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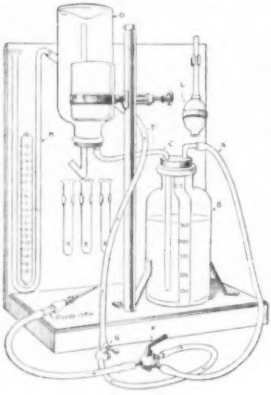

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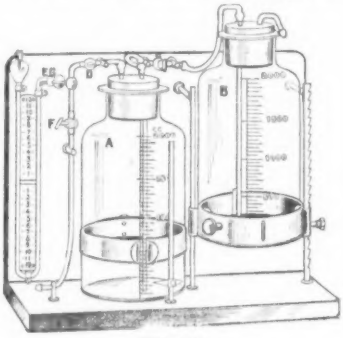

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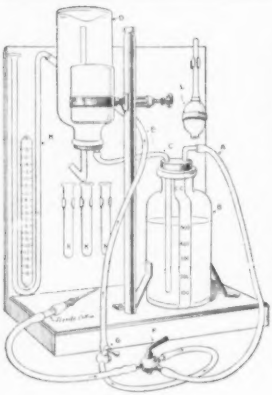

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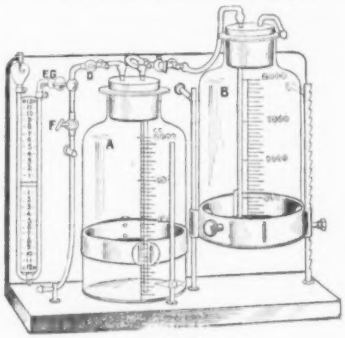

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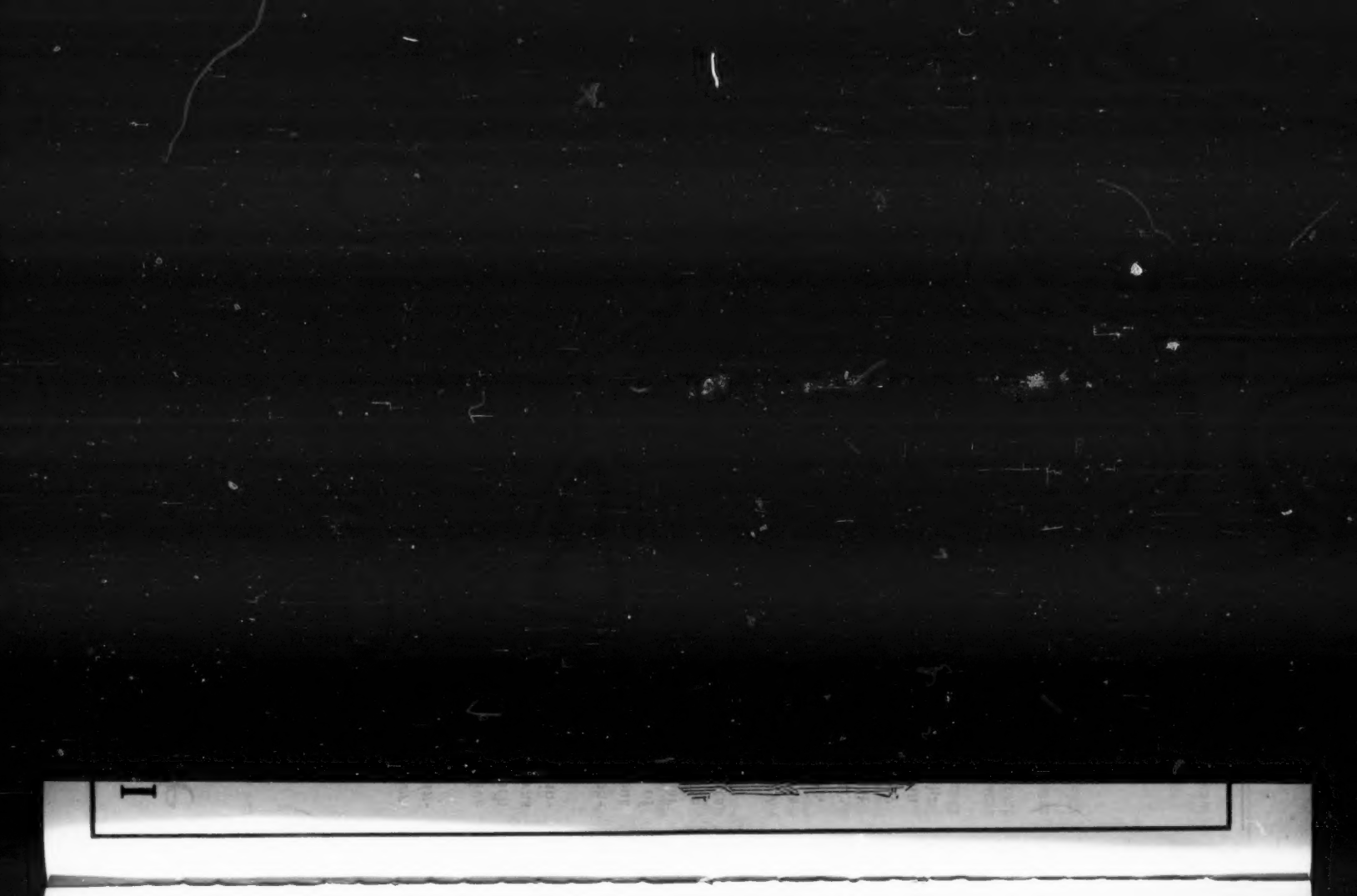

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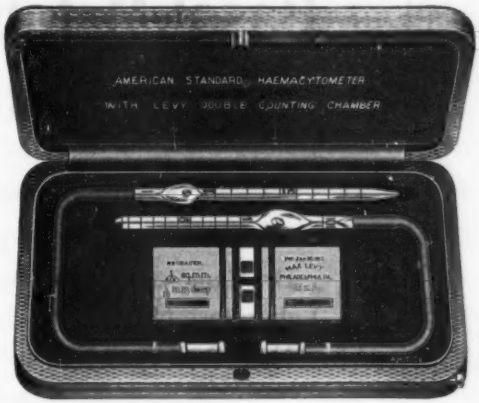

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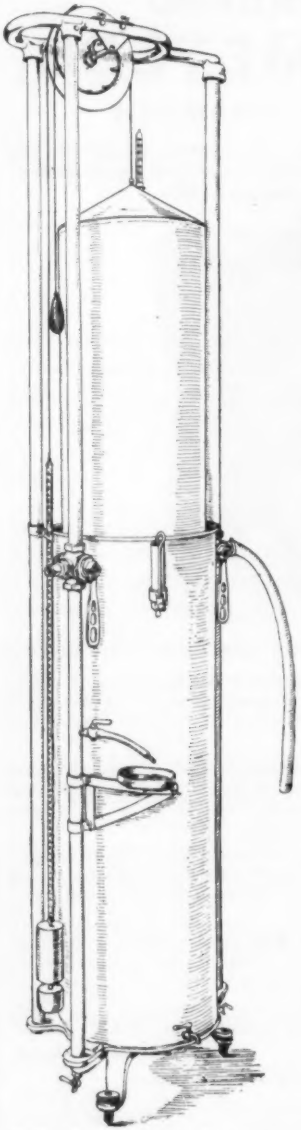

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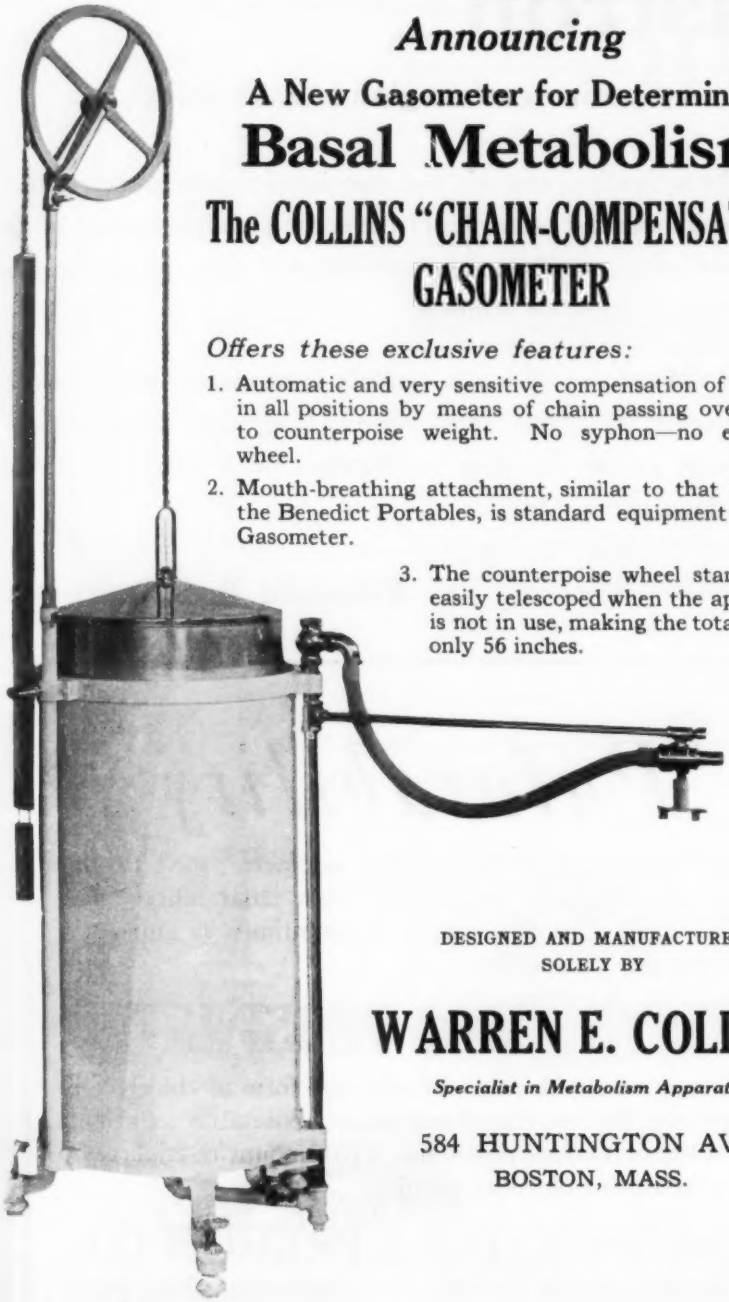

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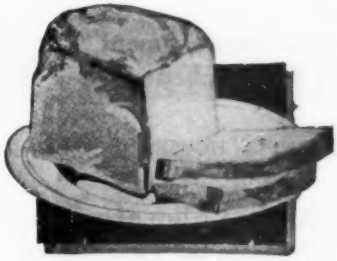

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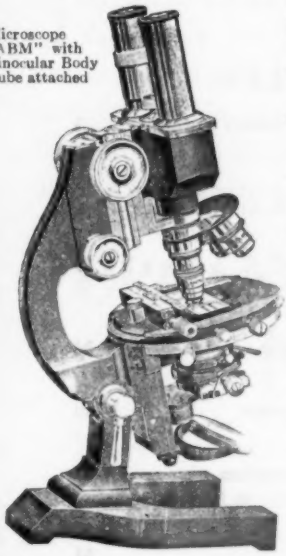

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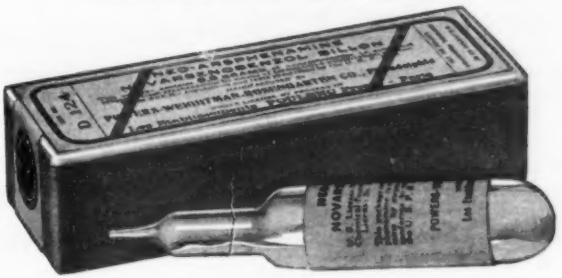

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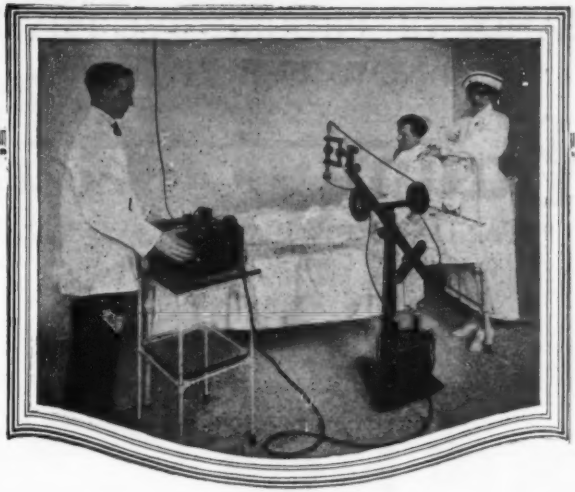

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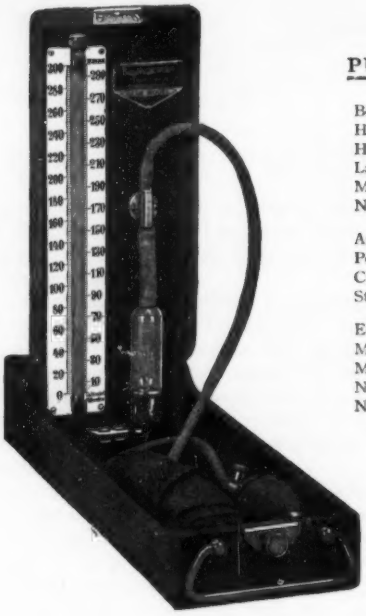

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JANUARY, 1923

ORIGINAL ARTICLES.

EFFECTS OF ACUTE AND CHRONIC PNEUMOTHORAX (A PRELIMINARY REPORT.)[1]

By J. L. Yates, B.S., M.D.,
MILWAUKEE, WIS.

Physiologists have cited the interdependence of respiration and intrapulmonary circulation as a nice example of coördinated functions. Indeed, so intimate is this interdependence that the degree of integrity of the pulmonary circulation compared to normal, directly or indirectly measures not alone intrathoracic function but also pleural and pulmonary powers of defense and repair. Consequently the ultimate evaluation of intrathoracic therapeutic procedures can be estimated by the protection and rehabilitation assured to the lesser circulation.

Pneumothorax produces effects common to other forms of pulmonary deflation and compression, either intrinsic, due to exudates, transudates, neoplasms and chronic passive congestion (Drinker), or extrinsic, resulting from pleuritic effusions, mediastinal tumors, aneurysms and the like. Wherever intrapulmonary pressure exceeds intravascular tension a proportion of the blood destined under normal conditions to reach the compressed lung area is immediately diverted to adjacent channels offering less resistance. The capillary network that surrounds the air cells spreads, as its component vascular tubules are thus elongated by overfilling. If air passages are free and lung tissue is elastic, the result is increased inflation in the portion of lung to which extra blood has

[1] Read before the American Association for Thoracic Surgery, June 6, 1921, as part of a symposium on open pneumothorax.

been delivered, a compensatory physiologic emphysema. On the contrary a temporary stoppage of pulmonary circulation produces atelectasis; permanent stoppage causes atrophy in the lung affected. In short, the pulmonary circulation is the most important factor influencing pulmonary inflation, and fluctuation in pulmonary inflation is accompanied by variations in the resistance to blood flow in the pulmonary circulation. The richness of the bronchial arterial blood supply, somewhat proportionate to the size and activity of the lung except in extreme degrees of emphysema and possibly of collapse, can also be measured by the condition of the pulmonary circulation.

The occurrence of compensatory physiologic emphysema in human lungs has long been recognized by clinicians, though it is not always demonstrable post mortem because of failure of blood-pressure at death preceded by a gradual antemortem reduction. The extent of compensatory emphysema depends upon the area of lung compressed and upon the competence of the circulation. Gregoire noted a zone of emphysema about areas of hemorrhagic infiltration due to wounds of the lung which is comparable to similar changes to be found about early foci of bronchopneumonia. Skodaic resonance, so often present above an effusion, was found by Bradford, Soltau and others to be particularly noticeable in the presence of hemothorax and to be due to emphysema in the lung just above that compressed by the bloody effusion. Individuals who have a competent circulation and develop an extensive unilateral pneumonia or pleural effusion regularly show a contralateral emphysema. Surgeons who operated without differential pressure upon soldiers suffering from chest wounds noticed that men in good condition tolerated extensive thoracotomy with comparatively little respiratory distress, whereas those who were in shock were much embarrassed by lesser parietal incisions. Those operators who used positive pressure anesthesia observed that the reëstablishment of a more normal pulmonary circulation through pulmonary inflation usually resulted in improving the individual's general condition. Moreover, during operations, as the extent of pulmonary inflation was varied to give desirable exposure, two other observations were made: The extent of deflation that could be tolerated without distress was greater in the men in better condition, and when complete deflation was possible, the mediastinum instead of becoming convex toward the sound side actually became convex toward the open side. Many surgeons have noticed, when operating without differential pressure to relieve chronic empyema, that as the exudate upon the visceral pleura is incised the underlying lung tends to bulge outward.

The capability of increased pressure in pulmonary circulation to augment inflation in a compensatory fashion explains these reactions. The lung is in effect an erectile tissue. The part played

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by vasomotor control of the pulmonary circulation remains to be demonstrated.

Experiments are being conducted with the coöperation of Dr. William Thalhimer and Dr. Benjamin Schlomovitz to determine the influence upon defensive pleuropulmonary reactions of varied intrathoracic conditions and among them is artificial pneumothorax. We are unprepared to make final statements, as our observations are incomplete. Results thus far obtained have so direct a bearing upon acute and chronic pneumothorax that they are presentable as a part of this symposium.

Pneumothorax induced by injecting known amounts of air unilaterally into the chests of anesthetized animals produces effects that vary with the type and conditions of the animal and the rate of injection. Cats and dogs, animals of the thin pleura type, have mediastinums that are not air-tight. Man and monkey, thick of pleura, have air-tight mediastinums. Unilateral pneumothorax is possible in man and monkey and impossible in cats and dogs.

If air be injected gradually into the left pleural cavity of a dog, there is a bilateral decrease in the negative pressures, usually greater on the right side (Fig. 1). If the air introduced gradually is insufficient in amount to cause the negative pressure to disappear and then is withdrawn, there is an immediate return to the previous pulse and respiration rates, systemic blood-pressure and negative intrapleural pressure. Increasing pulmonary compression is met with rising blood-pressure and so long as the increment is adequate, respiratory distress, indicated by slower and deeper respirations, does not develop.

A more rapid introduction of air in amounts sufficient to abolish negative pressure leads promptly to respiratory embarrassment as the compensatory blood-pressure rise is insufficient to meet requirements. If more air be injected so as to create increasing positive pressure respiration will cease (Fig. 2). The blood-pressure falls as it becomes inadequate, the rapidity of fall being somewhat proportionate to the extent of compensatory failure. Sudden variations in the negative pressure may occur spontaneously during a period of considerable compression and result from changes in the distribution of blood in the pulmonary circulation (Figs. 1 and 7). These observations offer a probable explanation of the fluttering mediastinum occasionally observed during operations performed without differential pressure. When the air that has caused marked pulmonary compression is withdrawn rapidly, there is a tendency for the negative pressures to increase temporarily beyond normal levels instead of returning to normal as above described (Fig. 2). This transient excess in negative pressures is attributed to a decrease in the amount of intrapulmonary blood, the excess blood having been squeezed out by the compression.

It is soon reaccumulated and normal negative pressures reëstablished. As the animals' hearts become fatigued, the compensatory reactions become less adequate and respiratory distress appears more promptly and with less decrease in the negative pressures (Figs. 3 and 7).

Similar experiments performed upon monkeys produced significant results. If the animal is robust and the air be injected gradually, a positive pressure on the injected side amounting approximately to fifteen times the normal negative pressure may provoke a reduction of but three-fourths of the contralateral negative pressure (Fig. 4). So long as the blood-pressure rises sufficiently there is no respiratory distress. If, however, the animal be feeble or both feeble and fatigued, the reaction to unilateral pulmonary compression is similar to that of the dog (Fig. 5). In other words, with inadequate powers of cardiac compensation, compensatory contralateral emphysema does not occur and the animal reacts as if the pneumothorax were bilateral.

The effects of chronic pneumothorax have been studied only in the monkey. Apparently the compensatory emphysema is distributed irregularly through the contralateral lung and is present in patches even in the lung subjected to compression. This is because of irregularities in the distribution of blood. Although simple of explanation upon the basis of hydraulics, it may indicate the effects of vasomotor control. There is a thickening of the visceral pleura due to proliferation of the mesothelial cells of the serosa and the subserous elements which is very significant. Air is irritating to serous membranes and the long-continued effects of compression in the presence of an irritant makes for decreased pulmonary elasticity and therefore curtails normal respiration.

The following conclusions are based upon personal clinical experiences in caring for over two hundred soldiers suffering from intrathoracic injuries and upon many animal experiments not cited here. The list includes about one hundred and twenty-five soldiers upon whom open thoracotomy was performed. Differential pressure was used in ninety-three; the remainder were operated upon at the Ambulance de l'Ocean under ether anesthesia according to the teachings of Duval. During convalescence the progress in intrathoracic repair was studied when possible with fluoroscope and roentgen-ray pictures. All who died came to necropsy. There has thus been provided unusual opportunity to study the effects of acute and chronic pneumothorax and to compare the death rate, amount of distress and the duration of disability following thoracotomies performed with and without differential pressure. Experiments of the type cited in this communication have served to explain and to substantiate previous clinical and experimental observations.

Acute pneumothorax is dangerous in so far as it interferes with

the pulmonary circulation. The extent of the danger is determined by the integrity of the circulation, chiefly by the latent energy of the myocardium. Since reserve myocardial energy cannot be estimated accurately and is quite essential to life during a period of stress, open thoracotomy should be performed with some form of differential pressure. Thus alone may the degree of pulmonary deflation required for the intrathoracic operation be permitted to develop gradually, be controlled so as not to become excessive and allowed to be as transient as possible. The operation is incomplete until full pulmonary inflation is both obtained and maintained. The latter is possible only when suitable one-way primary drainage is used. Gas-oxygen positive pressure analgesia as developed by Gwathmey is simple, safe and satisfactory, and, in the absence of a negative pressure cabinet, is the best method now available.

Chronic pneumothorax, as well as chronic pulmonary compression by the pleuritic effusions inevitable after thoracotomy, must be avoided if surgeons would assure to patients the best chances for rapid, comfortable and complete recovery.

Experiments. Aspirating needles or small trocars attached to bromoform manometers were inserted obliquely through the third or fourth interspace so that only the tips entered the pleural cavity and were placed posteriorly and above the heart. The connection on the left side, provided with a two-way cock, permitted air to be injected or aspirated with a graduated piston syringe. Blood-pressure was recorded from a femoral artery by means of a mercury manometer. Fairly deep surgical anesthesia with ether was maintained throughout the experiments and as nearly as possible at the same depth. The possibilities for error were recognized, likewise the constancy thereof, so that they were held to be negligible since relative accuracy was sufficient for the purposes at hand.

The diagrams have all been reconstructed from kymographic tracings in the same way and are directly comparable. Time is measured as abscissas; 1″ equals two minutes; the ordinates indicate pulse, 1″ equals 160 beats; blood-pressure, 1″ equals 50 mm. Hg; intrathoracic pressure, right and left, 1″ equals 4 mm. bromoform; the amount of air injected or aspirated, 1″ equals 50 cc. The line marked ⊕ indicates atmospheric pressure.

Figure 1, *Dog* 5, *Observation* 1. The observation was begun with 100 cc of air already in the chest. A total of 300 cc was injected in thirteen minutes, which reduced negative pressures one-half and did not produce respiratory distress. The air was withdrawn at the same rate. The increased blood-pressure sufficed to provide compensation. Just before the total amount of air had been injected the negative pressure on the left side fell abruptly and quite as promptly returned to its proper level, an expression of a fluctuation in the pulmonary circulation. At the end of the experiment normal conditions were reëstablished.

Figure 2, Dog 5, Observation 2. A total of 400 cc of air was injected in eleven minutes, causing respiration to cease, and then it was withdrawn in two minutes. The dog was able to compensate temporarily with increasing blood-pressure until 350 cc had been

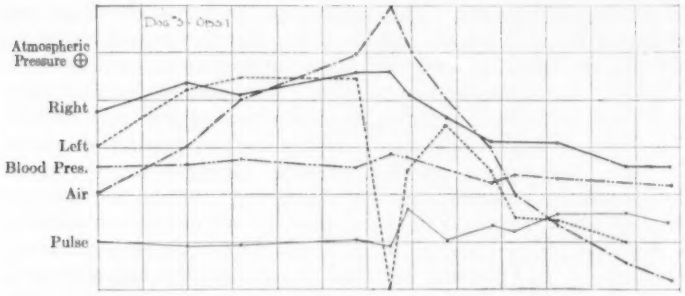

FIG. 1.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

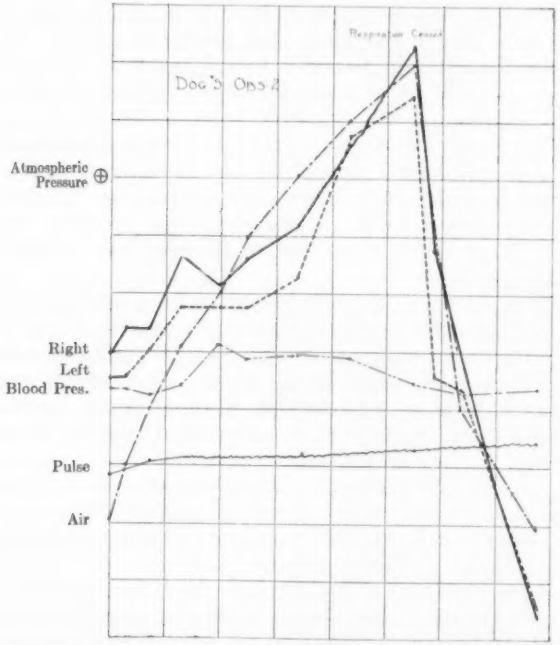

FIG. 2.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

injected even though there was positive intrathoracic pressure. Rapid removal of the air protected the blood-pressure from a material fall. The intrathoracic negative pressures at the end of the experiment were twice as great as at the start.

Figure 3, *Dog* 5, *Observation* 5. Between observations 2 and 5 two experiments were done. In each a cessation of respiration resulted when 350 cc were injected in three minutes. A repetition of the experiment shown in Fig. 2 proved that now 300 cc injected in five minutes caused respirations to cease, whereas before it required 400 cc in eleven minutes. There is now a decided fall in blood-pressure as compared to a slight fall in the former instance. A comparison of Figs. 2 and 3 shows the striking reduction in powers of compensation due chiefly to cardiac fatigue.

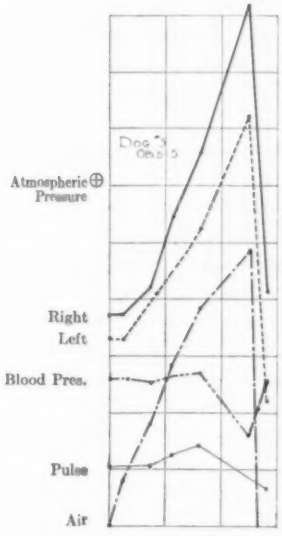

FIG. 3.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

Figure 4, *Monkey* 17. An injection of 150 cc of air in five minutes fell just short of provoking serious respiratory distress, though the fall in blood-pressure showed that to be imminent. The blood-pressure promptly rose with aspiration. The significant fact is that a positive pressure on the left side nearly five times as great as the amount of normal negative pressure reduced the right-sided negative pressure by only three-fourths. At the time when the left-sided pressure was atmospheric and equivalent to an open thorax, the negative pressure on the right side was reduced by

about one-half and respiration was unembarrassed. This explains why a thoracotomy can be performed without differential pressure in animals with a competent circulation in which the mediastinum is air-tight.

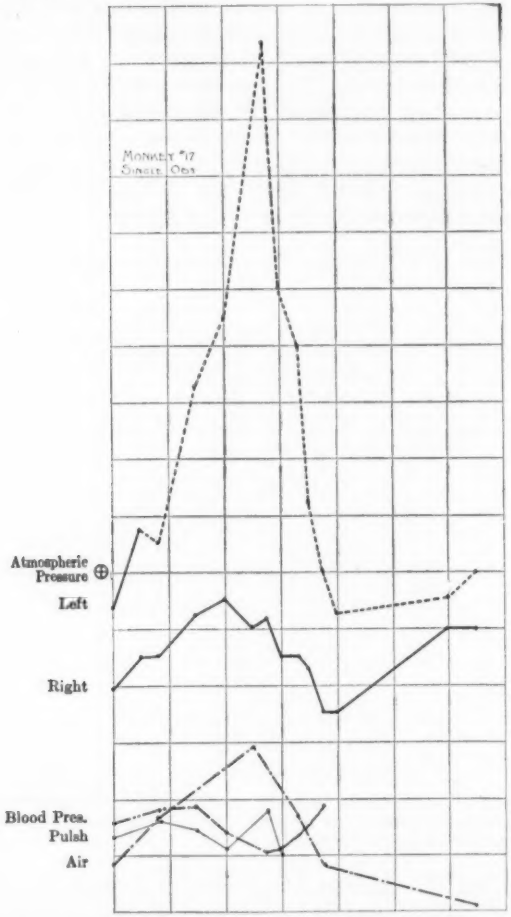

FIG. 4.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

Figure 5, *Monkey* 16, *Observation* 1. An injection of 150 cc in six and a quarter minutes caused respirations to cease, and in spite of prompt aspiration artificial respiration was required to save the animal's life. The striking feature of this experiment is to be

seen in the changes in intrathoracic pressures. Fifty cc of air in the left caused no change in the right side. Between 50 cc and 100 cc the right-side pressure rose rapidly but less rapidly than the left, and after 100 cc they rose even more abruptly. Monkey 16 responded more like a dog than like Monkey 17. Monkey 16 was an undernourished animal, unusually vicious and restive, and at the time the experiment was performed was considerably exhausted from fighting with its companions.

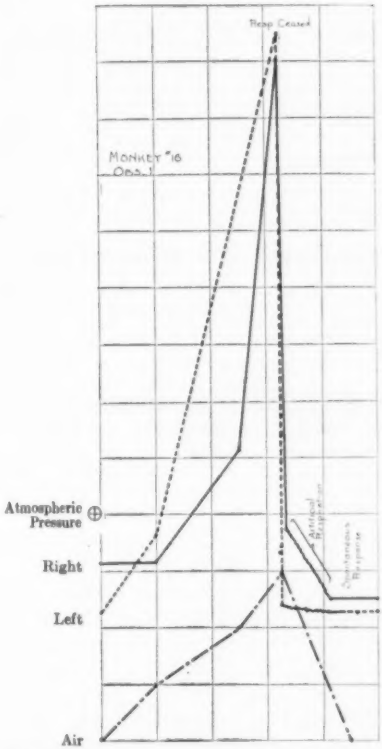

FIG. 5.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

Figure 6, *Monkey* 16, *Observation* 2. 150 cc of air injected in eleven minutes brought on respiratory distress. The more gradual injection of a smaller amount of air showed a more normal response in the intrapleural pressures and that respiration is temporarily possible in the presence of bilateral positive pressure.

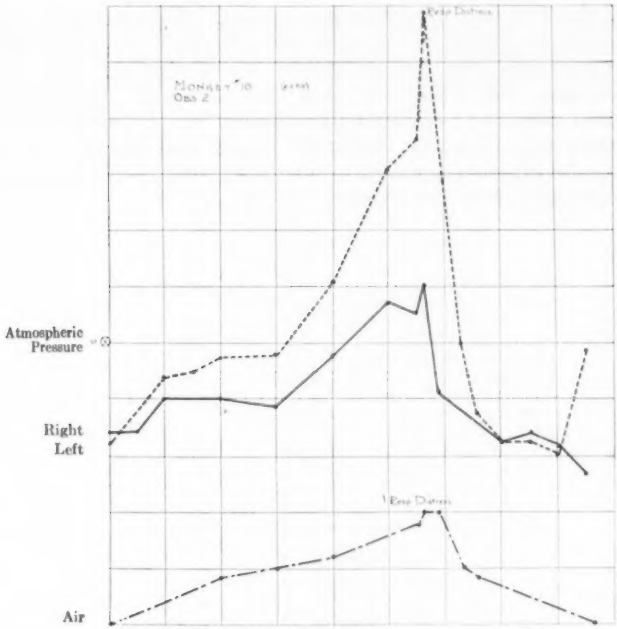

FIG. 6.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

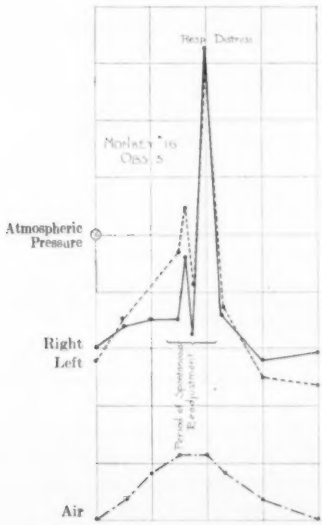

FIG. 7.—Abscissa, 1″ two minutes; ordinate, 1″ 160 beats; blood-pressure, 1″ 50 mm. Hg; intrathoracic pressure, right and left, 1″ 4 mm. bromoform; air injected or aspirated, 1″ 50 cc; atmospheric pressure ⊕.

Figure 7, *Monkey* 16, *Observation* 3. An injection of 60 cc of air in 3 minutes provoked cardiac instability that was followed after a minute by respiratory distress. A comparison of Figs. 5 and 7 shows an effect of fatigue similar to that illustrated in Figs. 2 and 3. The marked and sudden fluctuations in the intrathoracic pressures that occurred spontaneously are probably the cause of the "fluttering mediastinum."

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ANEURYSM OF THE HEPATIC ARTERY.[1]

By Julius Friedenwald, M.D.,
Baltimore,
and
Karl H. Tannenbaum, M.D.,
Chicago.

(From the Gastro-Enterological Clinic of the Department of Medicine, University of Maryland.)

Aneurysm of the hepatic artery is an exceedingly uncommon affection. Crisp in a study of 591 cases of aneurysm in general in 1847 does not refer to a single case of hepatic aneurysm. Mester in 1895 was only able to record 20 instances collected from literature and added a case of his own; Grunert in 1904 collected 36 cases; Schupfer in 1906, 38 cases, and Rolland in 1908, 40 cases. Weiss in 1921 described a case from McCrae's clinic in Philadelphia, which had previously been studied by McCrae himself, and was able to add 14 additional cases from literature, making 55 cases in all. Since then we have collected 9 additional cases not previously reviewed, and have added a case of our own, making 65 cases in all.

The following chart presents briefly an outline of the principal data of all the cases so far observed in literature. The scheme followed is that of Rolland, from whose chart we have abstracted the record of many of the first 40 cases.

[1] Presented at the Meeting of the Association of American Physicians, Washington, May 3, 1922.

No.	Date.	Author.	Publication.	Age.	Sex.	Number.	Size.	Position.	Immediate cause of death.	Etiology.	Symptoms.	Postmortem appearance.
1	1809	Wilson	Lectures on blood, etc., before Royal College of Surgeons, 1819, p. 379 (specimen now in Surgeons' Hall, Edinburgh)	50	M.	One	Resembles heart in size and shape	Left branch intrahepatic	Rupture	(?)	(?)	(?)
2	1820	Saint-Vincent	Arch. gén. de Chir., 1909, 122	51	M.	One	(?)	Main trunk	Rupture into peritoneal cavity	(?)	None	Abdomen filled with blood.
3	1821	Pitcairn	Specimen in Museum of Surgeons' Hall, Edinburgh, 36–296 (evidently unpublished)	48	M.	One	Hen's egg	Main trunk	Rupture into peritoneal cavity	(?)	None	(?)
4	1833	Sestie	Bull. de la Soc. Anat., tome **8**, 30	?	F.	One	Hazelnut	Right branch, extrahepatic	Exhaustion	(?)	"Chronic painful affection of liver"	Gangrene of gall-bladder.
5	1834	Stokes	Dublin Med. Jour., **5** 401	35	M.	One	Large orange	Main trunk, extrahepatic	Rupture into peritoneal cavity	(?)	Jaundice; hematemesis; slight pain; gall-bladder palpable	Abdomen filled with blood, due to rupture; aneurysm pressed on gall-bladder.
6	1834	Jackson	Med. Mag., Boston, **3**, 115	22	M.	One	Pullet's egg	Main trunk, extrahepatic	Rupture into hepatic duct	(?)	Pain; jaundice	Phthisis pulmonalis; old carotid aneurysm.
7	1855	Lebert	Anat. Path., **2**, 322	30	F.	One	Pigeon's egg	Main trunk, extrahepatic	Rupture into gall-bladder; marasmus	Embolic (?) typhoid and rheumatism	Pain; slight jaundice; hematemesis; melena; anemia	Old mitral endocarditis; old and recent pericarditis; enlarged liver; aneurysm did not rupture
8		Lebert	Quoted by Uhlig., Krankheiten der Arterien	..	M.	One	Hazelnut	Right branch	(?)	(?)	Gastric disturbance	(?)
9	1856	Ledieu	Jour. de méd. Bordeaux, p. 125	54	F.	One	Hazelnut	Main trunk, just above the origin of the pyloric artery	Albuminuria and general dropsy	(?)	None caused by aneurysm	Aneurysmal cavity quite occluded by very firm coagulum; cirrhosis of liver.
10	1856	Babington	Dublin Med. Jour.	25	F.	One	(?)	Main trunk	Rupture into duodenum	(?)	Sudden hematemesis; melena; epigastric pain	Blood in intestines.
11	1848	Wallmann	Virchows Arch., **14**, 389	36	F.	One	Child's head	Main trunk, 7 mm. above subdivision	Rupture into peritoneal cavity	(?)	Very severe paroxysmal pain; no fever, enlarged liver and spleen	Gall-bladder much distended.
12	1868	Uhlig	Inaug. Diss., Leipzig, 1868	48	M.	One	Goose's egg	Left branch, extrahepatic	Rupture into peritoneal cavity	Infective (osteomyelitis); atheroma (?)	Severe pain	Abdomen filled with blood.
13	1868	Kaufman	Inaug. Diss., Leipzig, 1868	48	M.	One	Goose's egg	Main trunk	Rupture into abdominal cavity	Arteriosclerosis	Attacks of abdominal pain; died in one attack	Enlarged liver; enlarged spleen; atheroma of arteries.

14	1871		Specimen in St. George's Hospital Museum (mentioned by Rolleston, Diseases of Liver, 1904, p. 44)	35	M.	One	Cricket ball	Main trunk, extrahepatic	Rupture into peritoneal cavity	Atheroma in aorta	Dead on admission to hospital	Adherent to small intestines.
15	1871	Quincke	Berl. klin. Wchnschr., p. 349	25	M.	One	Chestnut	Right branch; intrahepatic	Exhaustion from loss of blood	Infective	Severe pain; hematemesis; melena; jaundice; fever	Pneumonia; no rupture found.
16	1875	Standhartner	Berl. d. Wiener allg. Krankenheit.	23	M.	Two	(1) Walnut (2) Small nut	(1) Right branch; (2) left branch	Rupture of larger aneurysm into peritoneal cavity	Infective (?)	Icterus; high fever (not due to aneurysm)	Suppurative mediastinitis; pleurisy; pneumothorax.
17	1877	Ross and Osler	Canadian Med. Jour., 6	21	M.	One	Small lemon	Right branch, extrahepatic	Pyemia	Infective (?)	Those of pyemia	Double pleurisy; abscesses of liver.
18	1878	Borchers	Inaug. Diss., Kiel, 1878	17	M.	Two	(1) 2.2 cm. (2) 2.5 cm.	Intrahepatic	"Amputation of femur"	Infective (?) (osteomyelitis); trauma (?)	Pain; icterus; hematemesis; melena; fever	Ruptured into hepatic duct.
19	1878	Irvine	Trans. Path. Soc., London, 29, 128	45	M.	One	Small almond	Left branch, intrahepatic	Hemorrhage into stomach	Infective	Slight pain; hematemesis; melena	Stomach adhering and communicating with abscess of liver; early cirrhosis of liver.
20	1880	Drasche	Wien. med. Wchnschr., No. 37–39	27	M.	One	Hazelnut	Right branch, 1 to 5 cm. beyond division	Rupture into peritoneal cavity	(?)	Severe pain; hematemesis; melena	Abdomen filled with blood.
21	1880	Heschl	Quoted by Drasche	56	F.	One	Pigeon's egg	Main trunk just before division	Tuberculosis	(?)	None	(?)
22	1883	Weinlechner	Aerztl. allg. Bericht. der k. k. Krankenh. zu Wien.	Young	M.	One	(?)	Main trunk	Rupture into peritoneal cavity	Infective (?)	Sudden death	Recent osteomyelitis of femur.
23	1883	Chiari	Präg. med. Wchnschr., No. 4	33	M.	Three	Largest 2 to 1 cm.	Cystic artery	Rupture into gall-bladder	Cholelithiasis	Hematemesis; melena	Fistula between gall-bladder and duodenum.
24	1886	Caton	Clin. Soc. Trans., 19, 275	40	M.	One	1 inch in diam.	Main trunk, extrahepatic	Rupture into common duct	(?)	Intense pain; jaundice; hematemesis; melena; fever	Other organs healthy.
25	1892	Hale White	British Med. Jour., Jan., 1892, p. 223	18	M.	Two	(1) Tangerine orange (2) Slightly smaller	Right branch, extrahepatic; left branch, intrahepatic	Rupture of (1) into peritoneal cavity	Infective (?)	Pain; jaundice; hectic temperature	Pneumonia; empyema.
26	1892	Sachs	Deutsch. med. Wchnschr., 20, 443	60	M.	One	(?)	(?)	Rupture into portal vein; aneurysmal varix	(?)	(?)	Numerous gastric ulcers; portal thrombosis.
27	1893	Sauerteig	Inaug. Diss., Jena, 1893	31	M.	Two	(1) Apple (2) Cherry	(1) Right branch, extrahepatic (2) left branch, intrahepatic	Rupture of (1) into cystic duct	(?)	Severe pain; jaundice; fever; hematemesis; melena; enlarged liver	Operated on for cholelithiasis.
28	1893	Ahrens	Inaug. Diss., Greifswald, 1893	32	F.	One	Hen's egg	Main trunk	Rupture into peritoneal cavity	Infective	Collapse	Phlegmonous inflammation of leg; hematoma of hepatoduodenal ligament.

No.	Date.	Author.	Publication.	Age.	Sex.	Number.	Size.	Position.	Immediate cause of death.	Etiology.	Symptoms.	Postmortem appearance.
29	1894	Schmidt	Deutsch. Arch. f. klin. Med., **52,** 536	46	F.	One	(?)	Right branch, intrahepatic	Rupture into hepatic duct	Cholelithiasis; 13 stones	Pain; hematemesis; melena; jaundice	Perforations between gall-bladder and duodenum.
30	1894	Niewerth	Inaug. Diss., Kiel, 1894	19	M.	Two	(1) 1.8 to 3 cm. (2) cherry	(1) At the point of division; (2) main trunk	Rupture of (1) into gall-bladder and peritoneal cavity	Atheroma of hepatic artery	Partial obstruction of bowel; intense colic; tumor palpable	Cirrhosis of kidney; atheroma of aorta, etc.
31	1895	Mester	Ztschr. f. klin. Med., **28,** 93	42	M.	One	5 to 3.5 cm.	Right branch, intrahepatic	Rupture into hepatic duct	Trauma (kick of horse)	Pain; fever; hematemesis; melena; jaundice; operation by Miculiez; died in five days	Fatty degeneration of heart; bronchopneumonia; anemia.
32	1896	Sainton Bernard's Thesis 1897	Soc. Anatom., Paris, May	46	M.	One	Large orange	Main trunk	Rupture into peritoneal cavity	Diffuse atheroma	Slight jaundice; collapse; pain	Atheroma of aorta, etc.
33	1897	Hansson	Centralb. f. die Grenzgeb. d. Med. u. Chir., **1,** 299	14	M.	One	Hen's egg	Right branch, intrahepatic	Rupture into hepatic duct	Infective (?) (osteomyelitis	Hematemesis; melena	(?)
34	1900	Sacquepee	Zentralb. f. Path. Anat., **11,** 748	44	M.	One	Orange	Intrahepatic	Rupture into peritoneal cavity	Syphilitic endarteritis	Sudden collapse	Cirrhosis of liver.
35	1901	Brion	Deutsch. Aerzte Zeitung, No. 18	15	M.	Four	Cherry to pea size	Intrahepatic	Rupture and hemorrhage	Typhoid fever	Sudden pain; fever; melena; icterus	Necrotic areas in liver.
36	1902	Sommer	Präg. med. Wchnschr., **27,** 469	28	M.	One	(?)	Main trunk	Perforation into common duct	Infective	Icterus; pain; hematemesis; melena	Pneumonia; no atheroma.
37	1902	Sommer	Präg. med. Wchnschr., **27,** 469	65	F.	One	(?)	Point of origin of gastroduodenal artery	Rupture into duodenum and peritoneum	Trauma (fall)	No icterus; pain; fever; hematemesis	No atheroma.
38	1903	Kehr	München. med. Wchnschr., p. 1861	29	M.	One	Hen's egg	Right branch, extrahepatic	(Recovery after operation)	Pleurisy	Pain; jaundice; hematemesis	Aneurysm perforated into cystic duct.
39	1904	Grunert	Deutsch. Ztschr. f. Chir., **21,** 158	21	M.	One	Apple	Main trunk	Detected at operation for infection of gall-bladder (Habs, operator)	Infected gall-bladder; pneumonia	Hemorrhage; icterus; pain	Operation; gall-bladder full of infected bile; died eight days after operation.
40	1904	Sojecki	Inaug. Diss., Wurzburg, 1904	36	M.	One	(?)	Main trunk	(?)	Syphilis	(?)	(?)
41	1904	Riedel	Verhandl. Deutsch. Gesellsch. f. Chir.	31	M.	One	Apple	Right branch	Rupture into hepatic duct	(?)	Colic; icterus; hematemesis; tumor in gall-bladder region; operation	Hemorrhage; aneurysm contains numerous clots.
42	1905	DeVecchi	Bull. d. Science Med. di Bologna,	83	M.	One	Cherry	Right branch, extrahepatic	Cerebral hemorrhage	Gallstone	None caused by aneurysm	Jaundice; cerebral hemorrhage; granular kidney; gallstones.

43	1905	Libman	Proc. Path. Soc. News, 1905, **5**, 49	24	M.	One	Large	Right branch, intrahepatic	Acute endocarditis; pneumonia; streptococcic; septicemia	Infection	Only abdominal symptoms were diarrhea; poor appetite; cramp-like pain in abdomen; in addition mitral stenosis; acute endocarditis; mycotic aneurysm of right femoral artery; operated on for aneurysm of leg; streptococcic septicemia	Pneumonia in both lungs; vegetations in heart; several branches of superior mesenteric artery has several aneurysms, two the size of walnut, two the size of a bean; liver large and congested; fatty
44	1905	Schultze, 38	Ziegler's Beiträge, 38	57	M.	One	Apple	Main branch	Rupture into common duct	Gallstones	Colicky pain; jaundice; hematemesis	Hemorrhage into the bowel.
45	1906	Allessandri	Bull. d. Accad. med. di Roma, **32**, 63	22	M.	One	Hen's egg	Right branch, extrahepatic	Rupture into common duct	Infection (pneumonia)	No pain; no fever; jaundice; melena; liver enlarged; gall-bladder palpable; operation; tamponed aneurysm	Death six days after operation; hemorrhage.
46	1906	Livierato	Gazz. d. Osp. Milano, **27**, 593	28	M.	One	....	Main trunk	Rupture into peritoneal cavity	Infection (pneumonia)	Severe pain; vomiting; collapse	Double pneumonia; thrombosis of hepatic artery; liver healthy.
47	1906	Waetzold	München. med. Wchnschr., **43**, 2107	44	M.	Several	Largest a cherry, others smaller	Right branch, intrahepatic	Rupture into peritoneal cavity	Syphilitic endarteritis and periarteritis	Pain in liver region; those of cirrhosis of liver	Cirrhosis of liver; parenchymatous nephritis; endocarditis of aortic valve; necrosis of liver area.
48	1906	Schupfer	Gaz. d. hôp., Aug. 26, No. 102	38	M.	One	Hen's egg	Main trunk	Rupture into gall-bladder	Infection	Icterus; hematemesis	Hemorrhage into gall-bladder.
49	1907	Bickhardt and Schuman	Deutsch. Arch. f. klin. Med., p. 289	69	F.	One	Child's fist.	Right branch	Rupture into duodenum	Arteriosclerosis	Pain; pulsating tumor; vomiting; icterus; fever; hematemesis; osteomyelitis; pain; sudden hemorrhage; vomiting	Rupture and hemorrhage into peritoneal cavity; atheroma of aorta; hemorrhage into peritoneal cavity; swelling of liver cells; small abscesses of kidneys; coxitis.
50				10	M.	One	Hen's egg	Right branch	Rupture into peritoneal cavity	Embolic		
51	1908	Rolland	Glasgow Med. Jour., **69**, 342	46	F.	Three	(1) 25 cm. by 15 cm. (2) pea (3) barleycorn	Main trunk, intrahepatic	Rupture into abdominal cavity	Diffuse atheroma	Sudden pain in abdomen with collapse	Abdomen filled with blood; cardiac hypertrophy; chronic hepatitis.
52	1908	Reichmann	Virchows Arch., **104**, 71	26	M.	One	Pigeon's egg	Right branch	Rupture into abdominal cavity and bowel	Embolic	Colicky pain; fever	Thrombosis of aneurysm of hepatic artery.
53	1909	Tuffier	Presse méd., No. 18	72	M.	One	Goose's egg	Main trunk	Operation; ligation of artery	Obliteration; endarteritis	Icterus; pruritus; tumor in gall-bladder region	Patient died five days following operation; thrombus of artery partly calcified.

No.	Date.	Author	Publication.	Age.	Sex.	Number.	Size.	Position.	Immediate cause of death.	Etiology.	Symptoms.	Postmortem appearance.
54	1909	Bode	Beitr. klin. Chir.	23	M.	One	Walnut size	Right branch, intrahepatic	Operation, gastroenterostomy (Garre); death after eight days; rupture into duodenum	Trauma	Hematemesis; intense pain	Congestion and necrosis of small areas of liver.
55	1912	Dean and Falconer	Edinburgh Med. Jour., **8**, 124	22	M.	One	1½ to 1¾ inches, multilocular	Main trunk	Rupture into hepatic duct	Infection pneumonia	Icterus; hematemesis; melena; colicky pain; tender in epigastrium and gallbladder region	Rupture and hemorrhage; necrosis of area in right lobe of liver.
56	1912	Friedman	Med. Rec., Sept. 21, p. 522	35	F.	One	S-shaped; six inches in length	Main trunk	....	(?)	Alcoholic subject; pain; pulsation in liver region; systolic murmur and pulsation over liver; diagnosis made during life and confirmed by operation	
57	1913	Merkel	Virchows Arch., **214**, 289	56	M.	One	Hen's egg, 5 cm. long, 3.3 cm. wide	Main trunk	Carcinoma of stomach; operation; resection with gastrojejunostomy; sudden death ten days after operation	Trauma	None pointing to aneurysm	Hepatic artery entirely thrombosed and calcified; liver intact due to collateral circulation; chronic nephritis; chronic peritonitis.
58	1913	Fleckenstein	Inaug. Diss., Giessen, 1913	41	F.	One	Twice size of man's fist	Main trunk	Acute intestinal obstruction due to incarceration of intestine	Arteriosclerosis	Severe pain in abdomen	Aneurysm with many adhesions to the liver and portal vein; hepatic artery sclerosed.
59	1915	Baruch	Beitr. z. klin. Chir., **95**, 502	36	M.	One	Size of fist	Main trunk	Operation, pressure with tampon; died one day following operation from shock	Incipient arteriosclerosis	Jaundice; hemorrhages; fever; anemia	Hemorrhage into peritoneal cavity.
60	1916	Teacher and Jack	Glasgow Med. Jour., p. 277	43	M.	Three	(1) 4 by 25 cm. (2) very small (3) size of a walnut	Branch of hepatic artery intrahepatic	Rupture into abdominal cavity, chronic cardiac and nephritic disease	Probably syphilitic	Those of chronic nephritis with edema of extremities and cardiac disease; temp. to 102°; pain in liver region; died suddenly.	Intraperitoneal hemorrhage; periarteritis nodosa; thrombosus of aneurysm; chronic nephritis.

61	1919	Anderson	Tenn. Med. Jour., 12, 32	32	M.	One	....	Branch of hepatic artery, intrahepatic	....	Syphilis	Previous history of aneurysm of radial artery; pain; collapse; operation; laparotomy; 2 qts. of blood removed; sutures and packing; recovery; antisyphilitic treatment later; aneurysm of hepatic artery	
62	1919	Kading	Deutsch. Ztschr. f. Chir., 150, 82	35	M.	One		Intrahepatic, branch of hepatic artery	....	Trauma	Shot through liver and pleura; hemathothorax; pain in liver region; faintness; hematemesis; melena; 1st operation nothing accomplished; 2d operation a few days later (Sudeck); ligated hepatic artery; recovery	
63	1920	Hogler	Wien. Arch. f. inn. Med., 1, 509	51	M.	One	Walnut	Cystic branch of hepatic artery	Rupture into cystic duct; hemorrhage	Atheroma	Diagnosis made during life; systolic murmur over liver; colic; pain; hematemesis	Thrombosis of aneurysmal sac.
64	1920	McCrae	International Clinics, 3, 1	50	M.	One	2 cm. by 3 cm.; middle size of plum	Main trunk at point of division into the terminal branches	Rupture into abdominal cavity	Panarteritis of branches of hepatic artery	Acute abdominal pain; fever 100° to 102°; jaundice; tenderness in gallbladder area; died while taking anesthetic for exploratory incision	Chronic diffuse nephritis; granular degeneration of pancreas; obliterative endarteritis of small vessel of liver; aortitis; dissecting aneurysm of thoracic aorta and aneurysm of the left iliac artery.
	1921	Weiss	Am. Jour. Med. Sci., 161, 859									
65	1922	Friedenwald and Tannenbaum	Am. Jour. Med. Sci., 165, 11	48	M.	One	5 cm. by 4½ cm.; small orange	Extrahepatic	Rupture and hemorrhage into abdominal cavity	Panarteritis and atheroma of the hepatic artery and its branches	Jaundice; anemia; emaciation; hemorrhage; pain at termination	Endarteritis and atheroma of hepatic artery and its branches; rupture of aneurysm and hemorrhage into peritoneal cavity.

CASE HISTORY. H. L. F., male, married, aged forty-eight years, a merchant by occupation, consulted us on May 9, 1921, with the complaint of jaundice. His family history is essentially negative. His father died from nephritis; his mother is still alive and is well; two brothers and two sisters are living and are enjoying good health; while one brother died of nephritis.

Personal History. The patient's general health has always been excellent. He has had measles twice, but gives no history of any other infectious diseases or other illnesses. There was a small cyst removed five years ago from the outer surface of the upper gum in the midline by extracting the four central incisors and curetting the jaw. Healing proceeded normally following the operation and this affection has never since given him the slightest discomfort. The teeth are replaced by a removable bridge.

The patient was rejected from life insurance last fall on the ground of the finding of albumin in the urine. This was inconstant however, and was not revealed in two succeeding examinations. At that time the patient says nothing else abnormal was revealed.

Present Illness. About three months ago the patient began a course of dieting, being under the impression that he was too obese. He lost 12 pounds in weight in three weeks, and then began to feel a "bit out of sorts." He had indigestion following this occasionally, but of a mild type, and was affected with a slight diarrhea, but not with pain. The patient discontinued his reduction cure. He did not, however, feel quite up to normal, though he had no real complaint or discomfort. Eight weeks ago he began to notice a slight jaundice, which has gradually since been increasing. There has never been any pain and nothing abnormal was further revealed with the exception of a rather marked itching of the skin, bitter taste in the mouth, together with some loss of appetite, weakness, drowsiness and gradual loss of 18 more pounds in weight. The stools have never been clay colored, but are rather the reverse, darker than normal.

PHYSICAL EXAMINATION. The patient is a rather stout, well-developed man with a moderately deep jaundiced skin and sclerotics.

Head is of normal contour. Cheeks and eyes do not seem particularly sunken. Everywhere a marked degree of jaundice. Pupils round, regular and equal; moderately contracted; react somewhat slowly to light and accommodation. Extraocular movements are good. Ears and nose apparently normal.

In the mouth four upper incisors are missing and are replaced by a removable bridge. Beneath this is a well-healed scar of the operation on the gums, which leaves a rather marked depression in the center of the upper jaw, just beneath the septum of the nose. There is no infiltration of the gums about the scar. There is considerable dentistry. The tongue is coated with a brownish fur and protrudes in the midline; no tremor. The posterior pharynx

is moderately injected. The tonsils are small and normal in appearance. The neck is short and thick; no glands are palpable. The thyroid is not enlarged.

Thorax. The thorax is well formed; is rather broad and deep; some suggestion of barrel-shaping; expansion is good. The lungs are clear throughout to percussion and auscultation, except that the area of the liver dulness reaches up to just above the fourth rib, to the right, compressing the right lung slightly. The heart is not enlarged. The sounds are clear and of normal relative intensity. No murmurs can be made out. There does not appear to be any palpable degree of peripheral sclerosis. The pulses are of good volume and equal in force and rhythm.

Abdomen. The abdomen is full and thick walled. The edge of the liver can be palpated almost as far down as the umbilicus. The liver itself is rather smooth and not particularly tender to pressure and no nodules can be detected. The gall-bladder and spleen are not palpable. The lower abdomen is apparently normal.

Extremities. The extremities are normal. No glandular enlargements can be detected anywhere. The knee reflexes are present and are moderately active and equal throughout.

Laboratory Examinations. Total red count 4,200,000; hemoglobin 60 per cent; color index 0.71. Total leukocyte count 7500. Differential count: Polynuclears 57 per cent; small mononuclears 58 per cent; large mononuclears 3 per cent; eosinophils 1 per cent; basophils 1 per cent. Morphological examination negative with the exception of evidences of a secondary anemia. Serum bile tinged. The urine is of a specific gravity of 1025; presents a large bile ring and a few hyaline casts, but is otherwise negative.

The gastric contents; 60 cc obtained after an Ewald meal. Total acidity 34; free HCl 24; bile tinged; no blood.

Stool. The stool is almost tar colored, containing a few undigested meat fibers; no parasites; large quantities of blood.

Duodenal drainage according to the Lyon method revealed a markedly turbid bile which flowed freely; no gall-bladder bile obtained. Cultures showed numerous colonies identified as the colon bacillus. Fractional analysis of the pancreatic ferments according to the Einhorn method revealed an imperfect steapsin and trypsin digestion.

Roentgen-ray Examination. Stomach is of cow-horn type held to the right under the gall-bladder region; deformity surrounding the pylorus, suggesting a mass in the upper right quadrant. The liver is enlarged. Chest roentgen-ray is negative.

Diagnosis. On account of the age of the patient, his loss of flesh, absence of pain, jaundice, blood in the stools, diminution in pancreatic ferments, and the roentgen-ray findings, the diagnosis was made of carcinoma of the pancreas, though the possibility of a stone lodged in the ampulla could not be entirely ruled out.

CLINICAL NOTES. The patient was admitted in the Union Memorial Hospital, for further observation and possibly for operation, on May 15, 1921.

May 16, 1921. Patient was examined last night and appeared in good condition when last seen at 11 P.M. At 3 A.M., while on the commode, but before his bowels had moved, he had a sudden fainting attack. He lost consciousness and his pulse became imperceptible. This was associated with a very severe pain in the right hypochondrium just to the right of the epigastrium. The patient was revived after the administration of camphorated oil, although his pulse remained very weak and his respiration rapid; he was extremely pale and shocked. The pain in the epigastrium continued, though less severe than at the onset. Half an hour after the collapse the patient had a profuse bowel movement, but there were no evidences of blood clots or hemorrhage. Following this there was a second partial collapse, which was again relieved by the administration of camphorated oil.

During the remainder of the night the patient remained in a more or less shocked state, but had improved somewhat by morning. The pain in the epigastrium gradually subsided until now there is but little remaining. The medication consisted in the application of an ice cap to the epigastrium; morphine gr. $\frac{1}{4}$, every four hours. Nothing was allowed by mouth with the exception of crushed ice. The pulse during this entire period did not exceed 90 beats per minute, and the rate this morning was 76; yet the pulse is extremely weak, and the patient appears exsanguinated. The temperature is subnormal, 96.8°; respirations, 22. There is no evidence whatever of any lung complication. A transfusion of 500 cc of whole blood was given in the afternoon; no reaction was noted. At night the patient feels and appears much improved. The bowels have not been evacuated during the day. There is neither nausea nor vomiting. Nothing abnormal can be detected on palpation at the site of the pain. The abdomen is soft; there is neither tenderness nor rigidity. The attack remains unexplained.

May 17, 1921. Patient had a comfortable night; slept brokenly. Pulse is of good quality, about 50 per minute. Temperature 97°, respirations 20. He is allowed a slightly increased diet together with water. He was nauseated once in the afternoon, but did not vomit; there are frequent eructations following the ingestion of fluids. Large amounts of flatus are expelled. The bowels have not been evacuated in spite of a water and glycerine enema. The temperature rose to 100° in the evening. The patient has voided but 250 cc of urine since the attack, now almost forty-eight hours. He is perspiring almost constantly. His condition appears improved, although there is still no explanation of the attack, except the possibility of an internal hemorrhage not uncommonly observed in jaundiced individuals.

May 18, 1921. The patient passed a comfortable night. He has been annoyed at times by hiccoughing. He has voided urine very well since midnight. Some blood-tinged mucus has been expectorated this morning, due apparently to a general oozing from the nasopharynx rather than from a single bleeding-point; a slight cough has appeared this afternoon. An examination revealed the abdomen to be soft without tenderness. The borders of the liver extend to the umbilicus, and up to just above the fourth rib.

The lung is much compressed in this area but is resonant. A very loud coarse to-and-fro rub is heard over the whole front of the right chest, extending through to the back. Calcium lactate was prescribed in an effort to control the bleeding. The patient appeared quite comfortable and in an improved condition, except for the rub over his right lung. The patient has been ordered for operation in the morning.

May 19, 1921. A comfortable night was passed by the patient. At 8 A.M. his temperature was 98°, pulse 86, respiration 20. At 8.15 he suddenly uttered a cry, became pulseless and died. The diagnosis of hemorrhage was arrived at, the cause of which was not ascertained.

AUTOPSY REPORT. May 19, 1921. A partial autopsy only was permitted. The peritoneal cavity was opened through a high right rectus incision. The peritoneum was everywhere of dull appearance, the normal glistening quality being absent. About 2 liters of blood escaped on incising the cavity. Blood clots in large amounts were removed from the right side of the abdomen. The stomach and duodenum were inspected and found to be normal in appearance. The liver was much enlarged, and somewhat of a pale yellowish color, apparently fatty. The gall-bladder was slightly distended and contained a dark viscid bile but no stones. A mass was observed attached to the inferior surface of the liver posteriorly and adjacent to the gall-bladder. It appeared to be just anterior to the common duct. The mass was about the size of a small orange and presented a perforation on its anterior surface from which blood oozed following manipulation. The mass, together with the pylorus, part of the duodenum, portion of the abdominal aorta with the celiac axis and common bile duct, was removed.

The mass is an aneurysm of the hepatic artery. It is 5 cm. in length by 4.5 cm. in width and shows a perforation in its anterior surface 1.5 cm. in length from which it is evident the blood has escaped into the peritoneal cavity. The hepatic artery widens as it enters the aneurysmal sac, having a diameter of 2.5 cm. at this point. The interior of the aneurysm is partly filled with clotted blood extending into the branches of the hepatic artery. The jaundice noted can be easily explained on the basis of pressure of the aneurysm against the hepatic and common ducts.

A microscopic examination made by Dr. Standish McCleary is as follows: Sections made from the sac adjacent to the point of rupture show laminated fibers lying upon a much thickened hyaline intima. The medium as such has disappeared and is represented by an atheromatous mass containing many fat-laden phagocytes. There is also present a deposit of minute masses of calcium. The adventitia is thickened and has attached to its outer surface a thin layer of normal hepatic tissues. There is not the slightest suggestion of a luetic process in the tissue. Sections were also made from several of the smaller branches of the hepatic artery, and all show well-advanced endarteritis and in some cases early changes in the media.

Pathology. According to Mester, aneurysms of the hepatic artery may be divided into two groups, the extra- and the intrahepatic forms. Of these, according to this author, the extrahepatic is four times as frequent as the intrahepatic, while Rolland following the same classification finds it three times as frequent. In one collection of all cases previously recorded, in addition to our own case, numbering 65 cases in all, there were 45 extrahepatic and 18 intrahepatic, while in 2 both intra- and extrahepatic aneurysm were noted, as was observed in Sauerteig's and Hale White's cases, in which the right branch revealed an extrahepatic aneurysm and the left branch an intrahepatic.

In 60 of our 65 cases the main trunk was involved in 29 instances, the left branch in 6 and the right in 23; in 2 instances the aneurysm was noted as a part of the cystic artery (Chiari and Hogler). Two aneurysms were observed in 5 instances (Standhartner, Sauerteig, Borchers, Hale White, Niewerth). In Chiari's, Rolland's, and Teacher and Jack's cases there were three and in Waetzold's several. Aneurysms usually form adhesions to surrounding tissues, hepatic duct, cystic duct, gall-bladder, common duct, or surface of the liver, and finally rupture occurs into the organs to which there has been adhesions or into the peritoneal cavity which may thus be the immediate cause of death; usually repeated hemorrhages, however, occur, the blood causing a coagulum in the sac which seals the opening temporarily.

Of the 65 cases rupture of the aneurysmal sac occurred in 45 while 13 remained unruptured. The rupture was most commonly noted into the peritoneal cavity. In 33 instances of this series it occurred into the abdominal cavity, in 21 into the bile passages and in 4 into other organs, the stomach in 1, the duodenum in 2 and the portal vein in 1. When in intrahepatic aneurysms rupture occurs into the abdominal cavity, it takes place through the liver and is accompanied by a stripping of Glisson's capsule. Sacquepee was the first to note the importance of rupture of an intrahepatic aneurysm as the cause of rupture of the liver. Similar observations have been reported by Waetzold, Wilson and Rolland.

Occasionally the aneurysm may undergo spontaneous healing as was noted in Ledieu's case where the patient died of renal disease and in whom an aneurysm of the hepatic artery was demonstrated, occluded by a thrombus and which had not produced any symptoms whatsoever.

In Merkel's case the patient died ten days following a resection of the stomach and gastrojejunostomy. At autopsy an aneurysm of the hepatic artery the size of a hen's egg was discovered entirely thrombosed and calcified which too had not produced any symptoms.

The aneurysmal sac is usually single, though in 2 cases (Borchers and Niewerth) it was divided into two parts.

In 10 cases of this series the aneurysm itself was not the immediate cause of death (Lestie, Heschl, Ledieu, Ross and Osler, Grunert, DeVecchi, Libman, Quincke, Merkel, Fleckenstein).

The size of hepatic aneurysms varies from that of a barleycorn (Rolland) to a child's head (Wallmann), the average being that of a hen's egg. The extrahepatic forms are usually larger than the intrahepatic.

Etiology. This disease is more common in males than females. According to Hogler the incidence in males to females is as three to one, and according to our own observations as four to one.

Of the 63 cases in which the sex is recorded 50 were males and 13 females. The ages of the individuals affected range between the fourteenth year (Hansson) and eighty-third year (DeVecchi); the average age of the 63 cases is thirty-eight years; the average age of the males being thirty-six and females forty-four years; females are evidently as a rule affected in a later period in life. According to Rolland occupation plays but an insignificant role in the etiology of this affection, the disease being met with in individuals following the most diverse vocations.

As etiological factors in the production of this disorder infectious processes play a very significant role. Of these, strangely septic endocarditis, typhoid fever, pneumonia, osteomyelitis are far more frequent than syphilis. In many instances infective emboli are probably the cause, following such infections as endocarditis and suppurative processes. In a small proportion of cases syphilis is a factor. According to Grunert 73 per cent of the 36 cases collected by him were due to infectious processes.

Trauma has been considered in some instances as a causative factor in the production of these aneurysms, which may not only act from without but also from within, as by the direct injury against the arterial wall by gallstones.

In a number of instances of aneurysm embolism occurred as a result of endocarditis, while a certain number of cases were directly due to such infections as pneumonia, typhoid fever, osteomyelitis, pleurisy and empyema. In a not inconsiderable number atheromatous changes of the aorta and other vessels were observed. In

vegetative endocarditis emboli may be thrown off and caught in the arteries. Such vegetations ordinarily contain staphylococci and streptococci. At the position of the embolic thrombus there is at first an exudative inflammation produced, then an acute periarteritis with destruction of the media and the adventitia, and the intima bursts. As the result of these lesions, there is a bulging of the vessel and in the wall of the dilatation all layers of th rterial wall are to be found.

In Chiari's and Niewerth's cases atheroma was noted in the hepatic artery itself, but was also observed in many of the other bloodvessels, so that certain local conditions must be at hand to determine the production of the hepatic aneurysm. In some instances this may be in the form of a cholelithiasis on account of which direct injury to the weakened artery must be considered. In syphilis there is an intense endarteritis with visible damage to the arterial wall together with changes in the surrounding connective tissue. This affection was present in Sacquepee's, Waetzold's, Rolland's, McCrae's, Teacher and Jack's, Anderson and Sojecki's cases. Trauma as a cause of aneurysm was noted by Mester, Sommer, Sauerteig, Brion, DeVecchi, Merkel, Bode and Kading. In Sommer's case the patient fell in the dark and injured himself in the abdomen. In Mester's case a kick in the abdomen by a horse was noted as the cause. In Brion's case the patient was subjected to frequent pressure on the abdomen with bars of iron during his work.

In this series of 65 cases a definite causative factor was noted in 50 instances. Of these a general infection was observed in 7; typhoid fever in 2; pneumonia in 5; pleurisy with empyema in 1; osteomyelitis in 3; arteriosclerosis in 12; cholelithiasis in 5; syphilis in 7; trauma in 8 cases.

Symptoms. The symptoms most frequently observed in aneurysm of the hepatic artery are pain, hemorrhage, icterus, enlargement of the liver, fever, fluctuating tumor in the region of the gall-bladder, marked anemia, emaciation, together with attacks of syncope, dizziness, headaches, weakness and indigestion. All of these symptoms are rarely present in any individual case and ordinarily there are but few, in many instances the patient dying after a single attack of pain followed by hemorrhage without having had any previous symptoms whatever.

Pain. Of the symptoms noted above, pain is rarely absent and but few cases are recorded in which this symptom is not noted as an early and important sign. According to Schupfer it occurred in 70 per cent of his cases. It was present in 39 of the 49 cases of this series in which symptoms are recorded (79 per cent). Pain was extremely moderate in Stokes's and Irvine's cases and was entirely absent in Lebert's, Standhartner's, Ross and Osler's, Chiari's, Hansson's, Allessandri's, Schupfer's, Tuffier's, Baruch's and our

cases. In the case reported by us pain occurred but twice during the stage of hemorrhage at the very termination of the affection. The pain is usually paroxysmal, is of great severity, resembling biliary colic and is localized in the epigastrium and right hypochondrium in the region of the gall-bladder, descending according to Hogler

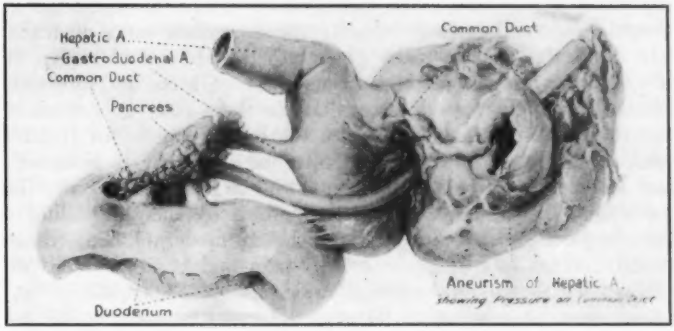

FIG. 1

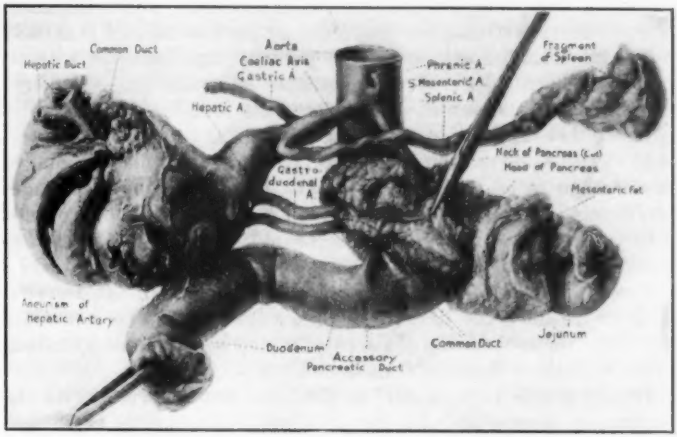

FIG. 2

toward the lower abdomen and back. It occurs rarely in the upper left quadrant (Irvine's case). In the intervals between the paroxysms pain is ordinarily absent.

The cause of the pain in the intrahepatic aneurysms is pressure on the liver capsule; in the extrahepatic forms to pressure of the aneurysmal sac on the hepatic plexus of nerves. During the attack

of pain tenderness on pressure is observed in the epigastrium and right hypochondrium.

Hemorrhage. Hemorrhage is a frequent symptom of this affection and is not uncommonly noted in the form of hematemesis or melena, or as both. Hemorrhages occurred in 31 of the 49 cases in which symptoms were recorded (63 per cent). They indicate rupture of the aneurysm, are often massive, intermittent, recur at irregular intervals, and are usually the immediate cause of death. The hemorrhages may take place into the abdominal cavity or bile ducts, or into the gastrointestinal tract. Gastric and intestinal hemorrhage is frequently occasioned in these cases as a result of the rupture of the aneurysm into the biliary tract. In Irvine's case, however, rupture occurred into the stomach; in Sommer's and Babington's into the duodenum and in Reichmann's into the intestine. Bleeding frequently checks itself by the rapid filling of the bile passages with blood. Even though moderate, hemorrhage usually occurs following the colicky pain and is associated with constitutional signs of weakness, rapid pulse and anemia.

Jaundice. According to Grunert, icterus was noted in 64 per cent of the cases of hepatic aneurysm and according to Schupfer in 62 per cent and to Rolland in 40 per cent. In this series of 49 cases in which symptoms were recorded, it occurred in 27 instances (55 per cent). It may be temporary or permanent and is usually increased with the attacks of the pain, though jaundice without pain has been observed in a number of instance. (Tuffier's, Baruch's, and our own cases). Temporary jaundice was noted by Quincke, Lebert and Mester. The jaundice is caused by the pressure of the aneurysm on the biliary passages or it may be due to hemorrhage from the aneurysm into the larger biliary passages producing obstruction by the formation of clots. The recurrent forms of jaundice are produced according to Bickhardt and Schuman by the latter condition.

Fever. A rise in temperature is occasionally noted. It occurred in 16 of this series of 49 cases, in which symptoms were noted (32 per cent), though in some of the cases it may be explained by causes other than those due to the aneurysm.

It may rise as high as 103° or 104° and usually occurs with the paroxysms of pain and may be associated with chills. Fever was first noted by Quincke in his case and occurred in Standhartner's, Ross and Osler's, Borchers's, Caton's, Hale White's, Sauerteig's, Mester's, Hansson's, Brion's Sommer's, Allessandri's, Reichmann's, Baruch's, Teacher and Jack's and McCrae's cases.

The rise in temperature has been compared by Quincke with that accompanying biliary colic and is probably due to infection or in some instances to the absorption of the blood following hemorrhage.

Tumor Formation with Enlargement of the Liver. Marked enlargement of the liver has been noted in a number of instances, especially

where the aneurysm had become massive. It was present in Sauerteig's, Wallman's and our cases. Distention of the gall-bladder was recorded in the cases of Stokes, Niewerth and Allessandri. In Stokes and Allessandri's cases it was due to pressure on the bile ducts and to the retention of bile in the gall-bladder and in Niewerth's it was produced by hemorrhage into the gall-bladder.

A palpable mass representing a hepatic aneurysm noted in the region of the liver was observed in the cases of Riedel, Bickhardt and Schuman and Tuffier. In Riedel and Tuffier's cases the tumor was nonfluctuant, while in Bickhardt's it fluctuated several days before death. While a nonpalpable mass was revealed in the cases of Friedman and Hogler, a visible pulsation was noted over the region of the liver associated with a systolic murmur. These signs lead to a correct diagnosis.

In addition to the symptoms already noted others more general, such as indigestion, anemia, emaciation, weakness, dizziness and fainting attacks have frequently been observed.

Diagnosis. The diagnosis of this affection is usually exceedingly difficult, as is evidenced by the fact that in but 2 cases of the 65 collected was the diagnosis correctly made during life except in those instances in which exploratory incisions were performed. The signs of colic resembling those of cholelithiasis, hemorrhage and icterus must be considered, especially when following upon such infectious diseases as pneumonia, typhoid fever and acute endocarditis. The diagnosis becomes more positive if a pulsating tumor is evident in the region of the liver exhibiting a systolic bruit.

In the differential diagnosis, cholelithiasis, duodenal ulcer and pancreatic carcinoma must be considered. In cholelithiasis there is usually an absence of hemorrhage and always of a pulsating tumor. On the other hand gallstones and aneurysm of the hepatic artery may occur in the same individual as was noted in Chiari's, Schmidt's, Grunert's and DeVecchi's cases, which may render the diagnosis even more difficult.

In duodenal ulcer the pain is not usually of the violent gall-bladder type, jaundice is usually absent and the roentgen-ray findings are ordinarily sufficiently suggestive to clear up the diagnosis. In carcinoma of the pancreas there is usually an absence of severe abdominal pain and large hemorrhages are unusual.

The average duration of this affection is from four and one-half to five months, the shortest being two months, as was noted in Borcher's case, and the longest eight and one-half months, as in Mester's case.

Treatment. Zesas,[2] who carefully reviewed the literature of this subject in 1910, concludes that ligation of the hepatic artery in cases of aneurysm is the only rational method of treatment and

[2] Fortschr. der Med., 1910, **28**, 1313.

maintains that there should be no delay in performing this operation once the diagnosis is established. Hogler very recently likewise arrives at a similar conclusion and points to the fact that Kehr was the first to perform this operation with recovery of his patient, establishing this operation as a justifiable surgical procedure. Previous to this period 3 cases were operated on with fatal results (Sauerteig, Niewerth, (Heller, operator), Mester, (Miculicz, operator), in none of which was the artery ligated.

On the other hand there has been considerable controversy regarding the propriety of ligating the hepatic artery in cases of aneurysm. Baruch refutes the advisability of performing this procedure from his experiments on thirty animals, and maintains that necrosis of the liver may result in consequence; according to his observations the more centrally the ligature is placed the less liable is this complication to ensue. Behrend[3] has also arrived at a similar conclusion from his experimental work on animals and has demonstrated that ligation of the hepatic artery terminates fatally, the interruption of the circulation resulting in an acute yellow atrophy of the liver with large areas of necrosis. Zesas, however, maintains, in opposition to this view, that animal experimentation differs in many respects from the actual conditions observed in human beings in whom on account of the length of duration of the affection sufficient time has elapsed for a collateral circulation to have thoroughly established itself.

Since the first successful operation performed by Kehr in 1903, 9 other cases have been subjected to surgery, the case of Riedel, Grunert (Habs, operator), Allessandri, Tuffier, Friedman, Merkel, Baruch, Anderson and Kading; of these but 3 recovered, the cases of Friedman, Anderson and Kading.

Finally it is interesting to note that of the 13 cases on whom operations were performed, on but 8 was the diagnosis correctly made at operation, the cases of Kehr, Grunert, Allesandri, Tuffier, Baruch, Friedman, Anderson and Kading.

Conclusion. It may be well to again draw attention to the fact that aneurysm of the hepatic artery is a rather rare affection, but 65 cases in all having been recorded; that the main symptoms of the diseases are colicky-like pain occurring in the region of the gall-bladder, hemorrhage and jaundice and occasionally a pulsating tumor exhibiting a systolic bruit; that ligation of the hepatic artery is the only rational method of treatment.

[3] Surg., Gynec. and Obst., 1920, **31**, 182.

FIBRILLATION OF THE AURICLE RETURNED TO NORMAL RHYTHM.

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It would seem advisable to study a few electrocardiograms of cases illustrating the return to normal rhythm in hearts which have been the seat of fibrillation of the auricle but were later normal in their auricular function. Some of the people with hearts of this type are under observation at the present time.

An excellent example is that of a man with extremely advanced circulatory disease, which is shown by an enormous enlargement of the heart, the maintenance of a terrific blood-pressure, the recurrence at various times of all the cardiac symptoms of heart failure, namely, dyspnea, edema, congestion of the lungs, liver and kidneys, and occasionally fibrillation of the auricle.

This man, nevertheless, now presents a fair appearance of health and a regular heart as the result of being put on a strict regimen. The only specific treatment he has been given for his fibrillation is digitalis. His normal rhythm is therefore a part of the natural history of the ups and downs of the auricle.

Another illustration of auricular fibrillation of an entirely different character is that of a man who developed cardiac disease as a result of long-standing, continued nervous strain and overwork. He had symptoms of angina pectoris. At the time of his examination he had auricular fibrillation. His heart is now regular as a result of his being put under a strict regimen.

The histories of the other cases are herewith described in detail with the electrocardiograms illustrating the return of rhythm to normal after auricular fibrillation.

Case I (LPIB).—A tall, stout man, single, aged forty-one years, weighing 200 pounds, came to the office complaining of palpitation. He had no precordial pain. His family history was negative and his personal habits were very good. He kept his bowels regular by daily doses of Russian oil. He gave a history of malaria seven years ago and rheumatism when thirteen years old, which, however, was apparently without cardiac involvement. He had had an attack of palpitation similar to his present one ten years ago. His present attack of cardiac palpitation followed influenza which he had four weeks previously. The attacks were best relieved by taking aromatic spirits of ammonia.

No marked abnormalities were found on physical examination. There were no heart murmurs and the pulse was regular on auscultation. The systolic blood-pressure was 120 and the diastolic

95. The blood picture was normal in every respect. Urinalysis showed no albumin and no sugar, but there were some leukocytes. It had a specific gravity of 1030. The Wassermann reaction was negative.

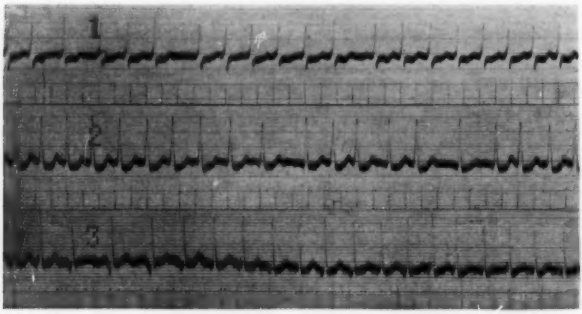

FIG. 1 (*a*).—Electrocardiogram showing auricular fibrillation, April 7, 1919.

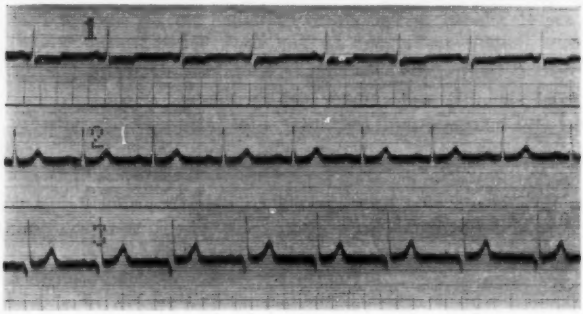

FIG. 1 (*b*).—Electrocardiogram showing return to normal rhythm without specific treatment, April 8, 1919.

CASE II (LISD).—A minister, aged forty-seven years, weighing 185 pounds, came for examination because of precordial pain on exertion. This pain occasionally extended down his left arm. His first attack of pain came on suddenly about a year previous to his coming here. He never had any attacks at night, but slept very well.

His family history was negative. His personal habits were excellent. Aside from recurring attacks of tonsillitis, he had had no former illness.

On examination a systolic murmur was heard several times over the aortic area, but no more definite signs were found. His systolic blood-pressure was usually 140 and his diastolic 100. The blood

picture was entirely normal and the Wassermann reaction was negative. Urinalysis revealed a faint trace of albumin and an occasional hyaline cast. The specific gravity varied between 1008 and 1028.

Under routine treatment with fortnightly doses of castor oil and careful dietary restrictions the symptoms have been greatly relieved during the succeeding two years.

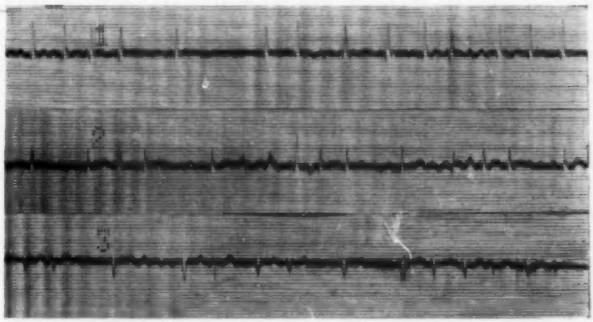

FIG. 2 (*a*).—Electrocardiogram showing auricular fibrillation, April 20, 1918.

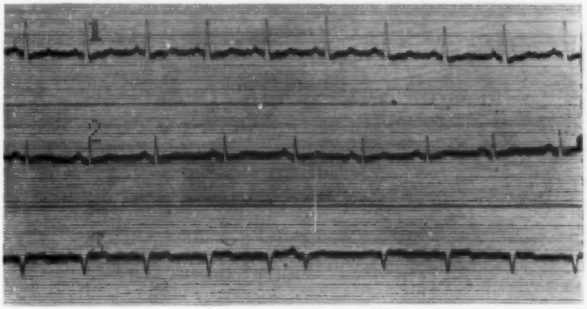

FIG. 2 (*b*).—Electrocardiogram showing return to normal rhythm without specific treatment, March 22, 1921.

CASE III (LOSL).—This man was a physician, aged forty-eight years, short and weighing 172 pounds. He complained of occasional skipping of the heart, giving him a peculiar feeling and a little dull pain. These symptoms had occurred during the preceding five years and seemed to have some relation to the eating of shell-fish and green peppers, as well as to excessive tobacco smoking. His family history was negative aside from the death of one brother from tuberculosis. His appetite was good and his bowels were regular, due, no doubt, in some part to the fact that he took plenty of daily exercise.

The only illness he had had was pneumonia when at college and occasional attacks of grip.

Physical examination on several occasions showed a soft systolic murmur both at the apex and over the aortic area. While under observation he suffered from an attack of auricular fibrillation, which was also verified by the electrocardiogram. The blood-pressure varied between systolic 115-130 and diastolic 90-95. On our advice his tonsils were removed. Following the attack of fibrillation ½ gr. of digitalis was given b. i. d. A week later the heart was greatly improved.

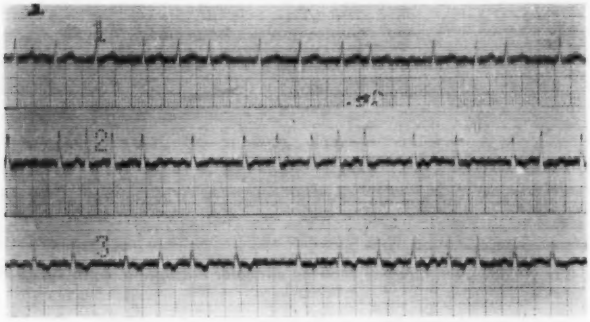

FIG. 3 (*a*).—Electrocardiogram showing auricular fibrillation, January 18, 1919.

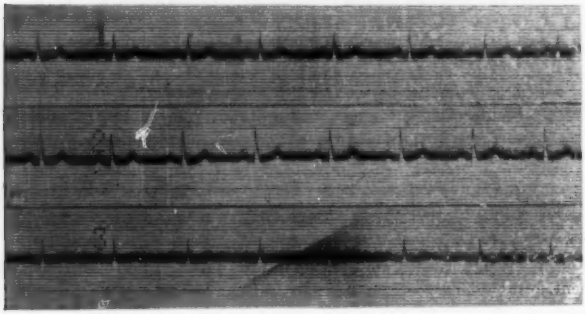

FIG. 3 (*b*).—Electrocardiogram showing return to normal rhythm, January 20, 1921.

The first urine examination showed a specific gravity which varied between 1024 and 1028. There was a faint trace of albumin, and in one specimen sugar to the extent of 1.6 per cent was found. Exactly two years later the urinary findings were entirely normal. The blood Wassermann was negative. The red and white cell counts and the hemoglobin were normal.

During the two years which have elapsed since this patient was

in the office he has had only four or five heart attacks, all of which were of very short duration. Since his tonsillectomy he has felt much better, but is unable to say whether this has had anything to do with the relief from heart attacks.

Under the regimen of fortnightly doses of castor oil he has had entire relief from his attacks and is able to exercise and go hunting as much as he wishes. He has noticed that the attacks usually follow either overeating or excessive use of tobacco.

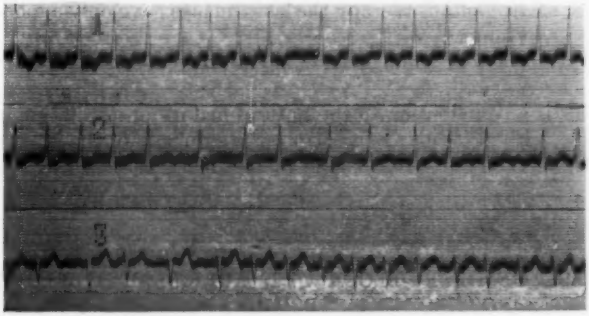

FIG. 4 (*a*).—Electrocardiogram showing auricular fibrillation, October 16, 1920.

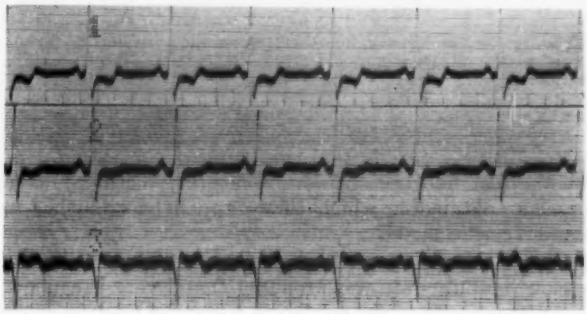

FIG. 4 (*b*).—Electrocardiogram showing return to normal rhythm, December 15, 1920.

CASE IV (IBIP).—A man, aged fifty-three years, weighing 175 pounds, single, came to the office complaining of dyspnea on exertion, pain and high blood-pressure. His personal habits were good. He abstained from tobacco, tea and coffee. His history revealed several attacks of rheumatism, measles and two attacks of pneumonia, twenty and five years ago respectively. His family history was negative except that his father died of Bright's disease.

His present complaint was of apparently rather short duration, having commenced three or four months previous to examination.

His heart was found to be very much enlarged, with a soft apical systolic murmur and marked accentuation of the aortic sound. His blood-pressure was very high, ranging between 250-220 systolic and 140-120 diastolic. The blood examination showed a very definite anemia with 80 per cent hemoglobin and 4,200,000 red blood cells. The Wassermann reaction was negative. Urinalysis revealed a marked amount of albumin with a moderate number of hyaline and granular casts. The specific gravity was 1015.

The first electrocardiograms showed the heart-rate to be regular. Under slight digitalis therapy the last tracings gave only a moderate sinus arrhythmia.

A month ago he complained of slight precordial pain on exertion.

This is a contribution to the natural history of fibrillation of the auricle, with particular reference to the emphasis of the importance of a careful appraisal of results of treatment in these people.

A CASE OF HEART-BLOCK AND AURICULAR FIBRILLATION WITH POSTMORTEM SPECIMEN; COMMENT ON THE ETIOLOGY OF FIBRILLATION.

By Selian Neuhof, M.D.,

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M. S., female, aged eighty years, was admitted to the ward August 7, 1920. Except that she entered the hospital acutely ill and that she had been in normal health prior to admission, no history was obtainable which threw any light upon her present illness.

The house physician made the following notes: "Shortly after admission the pulse-rate was around 150 and very irregular. The patient was cyanotic. She was given 1 dram of tincture of digitalis and $\frac{1}{100}$ gr. nitroglycerin every five minutes for one hour. (The total amount of the tincture thus administered was $1\frac{1}{2}$ ounces.) After a short time the cardiac rate dropped to forty per minute and gradually became slower until the rate was twenty-eight per minute. It remained at that rate for a few days, again gradually to increase to forty per minute. Upon admission she had an attack lasting two or three minutes, during which time breathing almost entirely ceased, and the pulse and heart action were scarcely perceptible. These spells were rather frequent during the first two days; they became less frequent, to disappear entirely on the fourth day." The patient died November 15, 1920.

I examined the patient for the first time about one week after admission. The heart action then was slightly irregular, the rate forty-five per minute. On the succeeding days and until the time of death, the ventricular rate remained between forty and fifty per minute. There were no cardiac murmurs. There was no edema of the legs. There were a few mucous rales at both bases. The patient was fairly comfortable and not very dyspneic. I took the first electrocardiogram two weeks after admission (August 21) and then another on November 10 (Fig. 1), one week before death. Both were alike and showed auricular fibrillation and heart-block (Fig. 1). As a terminal illness the patient developed lobar pneumonia, with fever ranging to 104° F.; during this period the pulse varied from forty to sixty-five per minute.

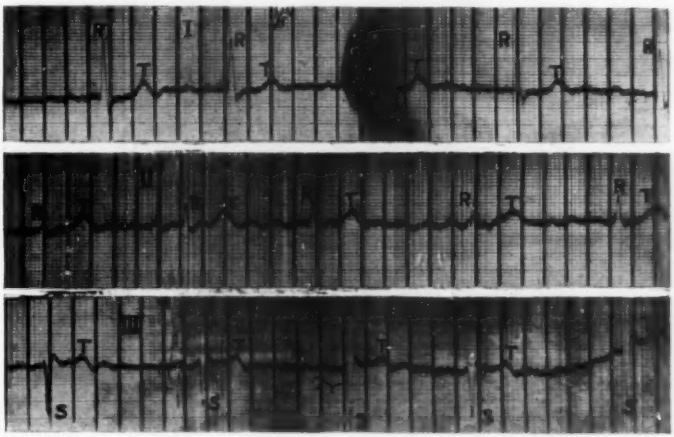

FIG. 1.—Typical section of a long electrocardiogram showing auricular fibrillation and heart-block. The ventricular action is slightly arrhythmic and the predominating rate is forty-six per minute.

Because the patient, a city ward, died without leaving relatives or friends, the heart could not be obtained for several weeks after her death. A bit of ventricular musculature was then excised, hardened and sectioned to discover whether the heart could still be used for microscopic study; it was found that the musculature was in too poor a state of preservation for such purpose. The gross pathology, however, was quite apparent, and it is questionable whether microscopic examination would have added anything of importance. The heart was slightly enlarged. The wall of the left ventricle was slightly thicker than normal; the right ventricle was abnormally thin toward the apex. The right ventricular cavity was somewhat dilated. There were small areas of thickening on the mitral cusps. There was surprisingly little inter-

stitial fibrous change throughout the entire musculature. The auricles were not enlarged or thickened. The region of the sino-auricular node—the pace-making area at the junction of the soperion vena cava and the right auricle—showed no macroscopic change; the artery of that node was not visible or palpable.

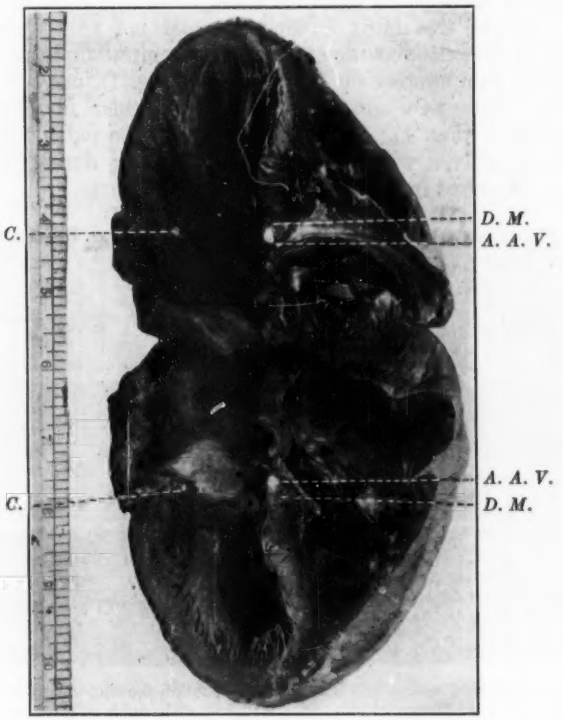

FIG. 2.—Photograph of the heart showing sclerosis of the coronaries (*C.*) and of the artery of the auriculoventricular node (*A. A. V.*). The artery is surrounded by a zone of degenerated musculature (*D. M.*).

The chief pathologic changes (Fig. 2)—undoubtedly the ones that finally caused the cardiac disturbance—were found in the coronaries, in the artery of the auriculoventricular node (the node of Tawara) and in the musculature surrounding the node. The coronary was thickened and sclerosed, although slightly patulous. The artery supplying the auriculoventricular node (the beginning of the auriculoventricular conduction system, the normal conveyer of impulses from auricle to ventricle) was completely calcified. The artery is seen occupying a position somewhat lower than the normal site of the node, but surrounding the artery (and probably as the result of its calcification) may be seen a distinct zone

of degenerated musculature (Fig. 2), which undoubtedly includes the node, either partly or entirely.

Comment. It is of great pathologic and clinical importance, especially in those suffering from what I may term impending "coronary failure," to note how long the final pathologic "insult" can hold off before complete occlusion of the coronaries or their subsidiaries occur. Undoubtedly the calcifying process in the coronary, and particularly in the artery of the node, had been going on for many years, yet the patient at the time of her death was eighty years old and had lived in cardiac comfort until sudden heart failure supervened; in all probability this resulted from final complete closure of the calcified artery supplying that node. This patient is but another illustration of the fact that the *slow* process of intracardiac arterial disease had never at any time sharply interfered with the factor of safety of the heart, and that ample time had probably been given for the establishment of coronary anastomosis; for, contrary to older teachings, it is now known that the coronaries are not end-arteries and that many deeply situated anastomoses exist.

Before proceeding to the clinical aspect of the case it may perhaps be well to recall certain pertinent physiologic attributes of the cardiac musculature. One of these is cardiac irritability. This does not depend upon the strength of the stimulus. It is, however, considerably influenced by other factors, especially by the state of nutrition of the cardiac musculature at the time of stimulation. Cardiac tissue is refractory to all stimulation during its period of contraction, hence the heart is irritable in the physiologic sense during its diastolic or resting period alone. Conduction, another important attribute, varies considerably in different parts of the heart; it is best in the specialized tissues—the sinoauricular node (the rhythm center) and the junctional tissue (the auriculoventricular conduction system).

The chief clinical interest in our case centers in the occurrence of heart-block and auricular fibrillation, but especially in the etiology of the latter. The heart-block is the cause of the slow ventricular activity. This is readily explicable from the gross pathologic changes—the calcified nodal artery and the myocardial changes in and near the atrioventricular node (Fig. 2). These focal changes undoubtedly destroyed the conducting function of the atrioventricular node. The massive digitalis therapy—$1\frac{1}{2}$ ounces of the tincture within one hour—may have been a factor in continuing the slow ventricular activity, although there is a definite note of the house physician stating that there were attacks of apnea with scarcely perceptible heart action (Stokes-Adams syndrome) upon admission. Nor does it seem probable that digitalis, even in such massive doses, could have had continued depressant action upon the ventricles during the remainder of the patient's life, approximately three months.

Regarding the auricular fibrillation we have no exact data as to its onset, except that the rapid and irregular pulse at the time of admission was probably indicative of this type of arrhythmia. Whether it had been present before hospital admission we do not know; from the obtainable history, however, there is no evidence of any prior attack of dyspnea or heart failure. Toxic causes (such as are encountered, for example, in exophthalmic goiter), reflex disturbances of the rhythm center from gastrointestinal disease, emotional disturbances, etc., need no consideration here as etiologic factors of the auricular fibrillation.

The possible causes of auricular fibrillation with heart-block in our case may perhaps best be discussed under the following headings:

1. Structural changes in the pace-maker.
2. Primary nutritional disturbances in the pace-maker.
3. Interference with and blocking of the normal spread of auricular impulses from a normally functionating pace-maker.

1. *Structural Changes in the Pace-maker.* Several observers (Cohn and Lewis,[1] Falconer and Dean,[2] Draper,[3] H. Freund[4] and others) had previously made careful serial microscopic examinations of the pace-maker and of the pace-making area in cases of auricular fibrillation with and without heart-block, and had ascribed decided etiologic significance to more or less extensive pathologic changes in the sinoauricular node. Such changes—usually degenerative and sclerotic in nature—where marked can undoubtedly cause auricular fibrillation. In some cases of auricular fibrillation, however, the sinoauricular nodal region was found normal or almost so. Hence where marked sclerotic changes are absent other causes for this arrhythmia must be sought. As above mentioned, macroscopic examination showed no evidence of any gross or extensive change in the pace-maker in our specimen.

2. *Primary Disturbances in the Pace-maker.* This would here refer practically to calcification and consequent occlusion of the artery of the pace-maker or to occlusion of one of the coronaries which occasionally gives off a branch to this node. The former change was absent in our case. Regarding the latter, while the coronaries were thickened and sclerosed they were still patulous, and hence would scarcely have interfered sufficiently with the arterial supply to the pace-maker, even assuming that a branch of the latter was given off by one of the coronaries.

3. *Interference with and Blocking of the Normal Spread of Auricular Impulses from a Normally Functionating Pace-maker.* Porter

[1] Auricular Fibrillation and Complete Heart-block, Heart, 1912–13, **4**, 15.

[2] Observations on a Case of Heart-block with Intermittent Attacks of Auricular Fibrillation, Heart, 1911–12, **3**, 247.

[3] Pulsus Irregularis Perpetuus with Fibrosis of the Sinus Node, Heart, 1911–12, **3**, 13.

[4] Klinische und Pathologisch-anatomische Untersuchungen über Arrhythmia perpetua, Deutsch. Arch. f. klin. Med., 1912, **106**, 1.

(quoted by Garrey) considers that "fibrillary contractions may be due to interruption of the contraction waves." Working independently, Garrey[5] and Mines[6] have shown experimentally that if the auricles be thrown into a state of fibrillation by direct faradization (the usual method), and if then a portion of auricular tissue (*e. g.*, the auricular appendix) be temporarily clamped off, fibrillation will continue in the remainder of the auricular tissue. When the clamp is removed the entire auricle again fibrillates. They have also found that if the auricle be incised trouser-fashion, so that sufficiently broad auricular strips remain connected by sufficiently broad auricular bridges and then the auricle be faradized anywhere, contraction of the various auricular strips will continue long after faradization has ceased. Garrey calls such contractions "circus contractions," for he assumes that such an excitation wave travels in a continuous circuit and that the impulse spreads from fiber to fiber. In the experimentally slit auricle these circus excitation waves are irregularly and sinuously blocked because of the difference in refractory periods of the incised fiber groups and because impulse conduction is interfered with. Thus while the circus excitation as an excitation impulse continues, the auricular strips are actually contracting at varying times and with varying energies. The result is incoördinate contraction, the irregular auricular tremor characteristic of fibrillation. Garrey also points out that "circus waves" are different from the normal in that the latter are large waves with rapid spread of the excitation; the reverse is true of "circus waves." Lewis and his co-workers[7 8 9 10] have recently corroborated Garrey's observations in a series of experimental and clinical papers.

The theory of Garrey and Mines seems to explain some clinical entities in which auricular fibrillation occurs frequently and in which an auricular mass as such may act as a factor. Thus in rheumatic mitral stenosis in which auricular hypertrophy and distention is common, and in cardiosclerosis in which accompanying sclerotic changes in the musculature are not infrequent, simple mechanical interference with the propagation of a "circus wave" may finally throw the auricle into fibrillation. My tentative interpretation in such instances is that there occurs mechanical hindrance to the spread of the excitation wave similar to what happens in the experimentally slit auricle; the excitation wave

[5] The Nature of Fibrillary Contraction of the Heart: Its Relation to Tissue Mass and Form, Am. Jour. Physiol., 1914, **23**, 397.

[6] On Dynamic Equilibrium in the Heart, Jour. Physiol., 1913, **46**, 349.

[7] Observations upon Flutter and Fibrillation, Heart, 1920, **7**, 127, 191.

[8] Observations upon Flutter and Fibrillation, Heart, 1921, **8**, 83.

[9] Further Observations upon the State of Rapid Reëxcitation of the Auricles, Heart, 1921, **8**, 311.

[10] A Demonstration of Circus Movement in Clinical Flutter of the Auricles, Heart, 1921, **8**, 341, 361.

cannot spread evenly and ripple-like because auricular conductivity and irritability are interfered with by the diseased or distended auricular strips; hence the excitation wave is irregularly and sinuously blocked and fibrillation results.

In addition to pathologic or mechanical changes in the auricular musculature, and excluding all toxic causes, it is of clinical importance to attempt a correlation of the theory of "circus waves" to disease primarily found not in the auricles but in the ventricles. It is, for example, no uncommon experience to find auricular fibrillation as a temporary or agonal arrhythmia with or without slow ventricular action in cases of coronary disease during an attack of occlusion (coronary failure), with or without pulmonary edema. Such sudden disturbance in intracardiac circulation with resultant impaired nutrition in the auricular musculature would seem sufficient to interfere with and impair the normal physiologic rhythmic excitation wave in the latter by producing local differences in the refractory periods and conduction time of the auricular excitation wave; thus a pathophysiologic basis for auricular fibrillation would be laid. In our case there was coronary disease with occlusion, the ventricles were beating automatically (heart-block) and the auricles were fibrillating. The possible influence of digitalis has already been discussed. Ordinarily in heart-block with coronary disease the auricles beat regularly and approximately at a normal rate. The assumption in such cases is that auricular nutrition is not sufficiently damaged to prevent the normal spread of impulses and excitation waves. Where auricular fibrillation occurs with heart-block the assumption seems fair that auricular disease or at least poor coronary circulation (coronary failure) so damages the entire intracardiac nutrition—auricles as well as ventricles—that auricular excitation waves are irregularly blocked similar to the blocking of the experimental "circus waves." As a result the auricles are thrown into that state of fibrillary contraction we designate clinically as auricular fibrillation.

THE ARSENICAL TREATMENT OF CHRONIC INFECTIOUS ENDOCARDITIS.*

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By the term "chronic infectious endocarditis" we refer to the group of cases known also as chronic malignant, or ulcerative

* Read at the Meeting of the Association of American Physicians, Washington, D. C., May, 1922.

endocarditis, running a course of three months to two or more years. This group is sharply distinguished from the chronic rheumatic endocarditis by the fact that the latter is associated with polyarthritis and by bacteria-free blood. It is convenient to separate this group also from the acute forms of infectious endocarditis, which present the clinical picture of acute septicemia. The organisms grown from the blood of these acute cases are the virulent strains of hemolytic streptococcus, pneumococcus, or gonococcus, while the organisms found in the blood of the chronic infectious type are the less virulent Streptococcus viridans or closely allied pneumococcus.

The diagnosis of chronic infectious endocarditis is somewhat difficult to make, because the patient is often up and about and may consult the physician only after weeks of malaise, weakness, slight fever, palpitation and loss of weight. Sometimes the occurrence of daily fever and sweats suggests tuberculosis; occasionally the development of abdominal tenderness and enlargement of the liver leads to a diagnosis of cholecystitis; frequently a high fever, enlarged spleen, and leucopenia simulate typhoid fever; or, in the absence of fever, the rapid pulse, sweats and loss of weight resembles a thyrotoxicosis. Later the true nature of the affection is revealed by the appearance of cardiac murmurs and emboli. When the emboli reach the brain, transitory loss of consciousness and motor symptoms may ensue; when they go to the spleen the organ becomes large and tender; when they affect the kidney, blood and albumin appear in the urine. Upon these findings the clinical diagnosis may be made, but the final proof rests with the recovery of Streptococcus viridans or pneumococcus, or rarely influenza bacillus in blood cultures. Skillful technic on the part of the bacteriologist and repeated examinations of the blood are essential in obtaining positive cultures. Even then according to Libman the majority of cases will yield negative results.

The purpose of this paper is to enter into a discussion of symptomatology only so far as it affects the diagnosis of the disease. The diagnosis established, our interest is in the prognosis and the result of various methods of treatment.

A review of the literature (Table I) brings out the frequency of an earlier and supposedly a healed rheumatic endocarditis. The mitral valves are most often involved, but the aortic may also be inflamed, either alone or in combination with the mitral valves. Blood cultures were not taken by the early observers and are not recorded by many recent writers. The positive cultures obtained show a marked preponderance of Streptococcus viridans, next in frequency the pneumococcus and a few scattered instances of influenza and staphylococcus.

TABLE I

Author.	No. of cases.	Duration of illness.	Blood cultures.	Organisms.	Specific treatment.	Deaths.	Recovery	Remarks.
1. Harbitz, 1899	16	4 to 8 mos.	.....	Pneum. 4 Strept. 9 Others 3	.....	16	0	All came to postmortem; noted healing process often.
2. Bartel, 1901	22	.....	.....	.....	.....	22	0	Noted healing valve lesions.
3. Lenhartz, 1904	16	3 to 7 mos.	.....	Pneum. staph.	.....	16	0	
4. Osler, 1909	10	4 to 13 mos.	3 + 3 0	Strept. 2 Staph. 1	.....	10	0	
5. Billings, 1909	14	3 to 14 mos.	All +	Strep. vir. 14	Autog. vaccine Ant. strep. serum	13	1	One well after seven years; thinks vaccine and serum useless.
6. Latham and Hunt, 1910	1	15 mos.	+	Coccus	Autog. vaccine by mouth	0	1	Thinks vaccine valuable.
7. Schottmüller, 1910	5	.....	.....	.....	.....	5	0	Reports 1 recovery; case died later.
8. Jochmann, 1912	7	.....	Some +	Strep. vir.	Autog. vaccine Ant. strep. serum	5	2	1 died on vaccine and serum. 1 well on vaccine and serum. 1 well on no vaccine and serum.
9. Libman, 1912–1920	150	3 to 18 mos.	+	Strep. vir. 95% Influenza 5%	.....	146	4	
10. Christian, 1918	2	.....	±	Strep. vir.	.....	1	?	1 living; too recent.
11. Starling, 1920	38	3 to 14 mos.	.....	.....	.....	35	3	Recoveries all recent cases.
12. Horder, 1920	150	.....	Some +	Strep. vir.	.....	149	1	
13. Münzer, 1921	1	15 mos.	+	Pneum.	Collargol Ant. pneum. serum	1	0	

Harbitz and Bartel both made important observations in large series of necropsies in chronic infectious endocarditis. They described even in these fatal cases evidences of healing of the valve lesions and suggested that recovery was possible.

In 1909, Osler stimulated a fresh clinical interest in the subject. Until the year 1885 he had seen only the acute types of septic endocarditis, all terminating in death within three months. From 1885 to 1909, he observed 10 cases of chronic infectious endocarditis, running a course from four to thirteen months and all ending fatally. He drew a clear picture of the condition, emphasizing the frequency of a previous rheumatic infection, the daily remittent fever, the petechiæ, the occurrence of emboli in the brain, kidney and retina, and the occasional development of characteristic painful nodular swellings under the skin. In six of his patients blood cultures were taken, three of which were negative, two showed streptococcus and one staphylococcus.

Soon after Osler's publication Billings reported 14 cases of the chronic type. The notable feature of his contribution was the success in securing positive cultures from the blood in every case, an achievement made possible by frequent and repeated efforts in taking cultures. In 11, Rosenow found pneumococcus and in 3 Streptococcus viridans, which may be considered as identical. Some of this series were treated by autogenous vaccines, and some by antipneumococcic and antistreptococcic sera. One patient of the 14 recovered, but she had received no specific therapy. Billings concludes that vaccines and serum therapy are of no value in treatment.

Schottmüller states that 1 of his 5 cases recovered, but this patient subsequently died of the disease (Libman).

Latham and Hunt record an interesting case with apparent recovery after fifteen months. Blood cultures six times yielded a growth of Gram-positive cocci and later they became negative. They attributed this result to administration of autogenous vaccine by mouth.

Jochmann says that in his experience chronic infectious endocarditis is caused almost exclusively by Streptococcus viridans, whereas the acute type is usually due to Streptococcus hemolyticus. He reports 7 cases with 2 recoveries. Three cases were treated with antistreptococcus serum, 1 of which recovered and 2 died. The other recovered patient received no specific therapy.

Libman (1912) as a result of a very extensive clinical and bacteriological experience states that the organisms responsible for chronic infectious endocarditis are Streptococcus viridans in 95 per cent and influenza and gonococcus together in 5 per cent of cases. He describes a large series with typical clinical picture, but in the "bacteria-free" stage. He believes healing of the valves does occur, "although the evidence of complete recovery from the clinical

side is still very meagre." "Nearly all cases in which we found bacteria in the blood went on to fatal termination with bacteria still in the blood. In but few cases did the blood cultures become negative and these patients also succumbed."

In a recent discussion (1920), however, Libman refers to 4 recoveries in a group of 150 well observed cases.

Starling recently referred to 38 cases of chronic infectious endocarditis, no mention being made of blood cultures. Three of these patients he considered had recovered, but sufficient time had not elapsed to settle this point.

Sir Thomas Horder in a discussion of 150 cases that had come under his observation says that the diagnosis of chronic infectious endocarditis rests on a triad of symptoms, viz., active endocarditis of chronic type, occurrence of emboli, and the recovery of streptococci in the blood. On any two of these symptoms the diagnosis may be made with reasonable certainty. Only 1 patient in his series recovered.

Münzer's case deserves mention because of his experiments with collargol injections which proved to be of no value.

Oille, Graham and Detweiler have made an interesting study of 8 mild cases of this disease. Three of the group developed arthritis, 3 had hematuria, 1 only exhibited a large spleen and none had petechiæ. In all, however, there was a distinct heart murmur and in every case the authors succeeded by the Rosenow method in growing Streptococcus viridans in blood cultures. The cases were so recent that the final outcome could not be included in the table. But the striking success in obtaining positive cultures in such mild types of the disease should be a stimulus to more intensive bacteriological studies in all suspected cases.

A summary of the results obtained in the combined series of Table I is as follows:

Of 419 cases reported 12 patients recovered, or less than 3 per cent.

Two of the 12 patients who recovered received vaccine. The remaining 10 cases received no specific treatment.

It is altogether probable that spontaneous recovery does occur in chronic infectious endocarditis, far more often than these statistics would indicate. The testimony of pathologists is that healed ulcerative lesions of the heart valves are not infrequently encountered at necropsy in persons dying of some other affection. Libman in particular has emphasized the likelihood of recovery in many cases that are never diagnosed.

Personal Observations. During the past twelve years we have treated all of our cases of chronic infectious endocarditis with daily injections of sodium cacodylate (usually intravenously), continued over a period varying from seven weeks to four months. In many of these patients we failed to find bacteria in blood cultures,

TABLE II.—OUTCOME OF CASES TREATED WITH ARSENIC

Name.	Period of observation.	Previous duration.	Prev. rheum.	Valves affected.	Temperature.	Blood.	Emboli.				Blood cultures.	Organisms.	Treatment.	Outcome.
							Spleen.	Kidneys.	Skin.	Elsewhere.				
R. T. L.	11½ yrs.	1 mo.	0	Mitral	99 to 100	H = 60 R = 3,020,000 W = 6,000 to 10,000	++	Alb. Blood casts	++	0	2 pos. 1 neg.	St. vir.	Sod. cacod. 10 wks.	Recovery
M. C.	5 yrs. 1 mo.	4 mos.	+	Mitral	97 to 100	H = 65 R = 4,100,000 W = 7,000	+	Blood casts	0	0	1 pos. 3 neg.	St. vir.	Sod. cacod. 4 mos.	Recovery
C. H. R.	5 yrs.	1 yr.	0	Mitral and aortic	98 to 101	H = 80 R = 4,800,000 W = 4,000 to 10,000	+	Alb. Blood casts	+	0	1 neg. 1 pos. 1 neg.	St. vir.	Sod. cacod. 7 wks.	Recovery
L. M.	2 yrs. 3 mos.	2 mos.	+	Mitral	97 to 101	H = 50 R = 3,420,000 W = 7,000	++	Alb. Blood casts	+	0	2 pos. 1 neg.	St. vir.	Sod. cacod. 2 mos.	Recovery
M. P.	5 mos.	9 mos.	0	Mitral	98 to 101	H = 64 R = 3,200,000 W = 9,000, to 10,000	+	Alb. Blood	+	Cutan. nodes	3 neg. 1 pos.	St. vir.	Sod. cacod. 12 wks.	Death
J. F.	15 wks.	10 wks.	0	Mitral	100 to 103	H = 84 R = 4,100,000 W = 12,000 to 18,000	+	Alb. Blood casts	+	Cutan. nodes Retina Hemipleg.	6 pos.	St. vir.	Sod. cacod. 3 mos.	Death
M. T.	6 mos.	8 mos.	+	Mitral and aortic	97 to 100.4	H = 76 R = 4,300,000 W = 7,600	+	Alb. Blood casts	+	0	2 neg. 1 pos. 3 neg.	St. vir.	Sod. cacod. 12 wks.	Improving
F. B.	5 mos.	1 mo.	+	Mitral and aortic	97 to 100	H = 85 R = 4,400,000 W = 7,000 to 13,000	0	Alb. Blood casts	0	Cerebral apoplexy	1 pos. 3 neg.	St. vir.	Sod. cacod. 3 mos.	Improving

although the other clinical findings were sufficiently characteristic for making the diagnosis. But for the purpose of determining the results of a specific therapy it seemed best to limit the present study to those cases alone in which the clinical evidence was corroborated by positive cultures from the blood. Eight cases were proven up by blood cultures and these are described in Table II.

The clinical features of these cases are so similar to the excellent descriptions of Billings, Osler and Libman that little detailed comment is called for.

Two of our patients died, and 6 survive. The duration of the disease in the fatal cases was six and thirteen months respectively.

The observation of the 6 surviving cases extends over periods of eleven years and six months, five years and one month, five years, two years and one month, six months and three months respectively. As the infection runs such a chronic course we can draw no conclusions from the last 2 cases. The remaining 4 cases having remained in good health for two years and more may be reasonably classified as recoveries.

The only specific therapy attempted was the prolonged use of sodium cacodylate in daily doses of 1 to 4 grains. The drug was pushed until a strong garlic odor was expelled with the breath. The preparations sold in the market in ampoule form are not very dependable, so that it is advisable to make a fresh preparation every few days of a reliable drug. No untoward effects were observed in any case. If the bowels became loose the dose was decreased for two or three days. Rest in bed was insisted upon during the period of treatment.

The results of blood cultures were of especial interest. Streptococcus viridans was the organism found in all cases.

In 1 fatal case six consecutive cultures were positive. In the second fatal case three negative cultures were followed by one positive.

All the healed cases showed the disappearance of bacteria from the blood during recovery. But it is never safe to give a good prognosis from negative cultures alone, since patients frequently die under these conditions.

Experimental Work. The experiments of Allison upon the effect of arsenic, in the form of a watery solution of salvarsan, diarsenol and arsenobenzol on streptococcus have an important bearing on the rationale of this treatment. "These preparations" he asserts "possess a distinct bactericidal power against virulent strains of streptococci in vitro in dilutions up to 1 : 3000, and an *inhibiting* power for at least twenty-four hours in weaker solutions. They possess bactericidal action against streptococci also in the blood stream of experimental animals. They produce no untoward effects on animals where large doses were frequently repeated. They possess hopeful possibilities for the treatment of streptococcus infections in human subjects as shown by limited human experience."

Our own experience with the arsenic treatment inclines us to believe that the drug in the ordinary dosage is "inhibiting," rather than bactericidal, and that it should, therefore, be given over a long period in order to bring about the death of the organisms.

We have employed cacodylate of soda because of its apparent safety, but other forms of arsenic may prove superior.

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THE FATE OF ARSENIC AFTER INTRAVENOUS OR INTRATHECAL INJECTION.*

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AND

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THE question of the fate of salvarsan, using the term salvarsan as a group one for all such arsenical preparations, after its intravenous injection is a large one and the work that is here presented only goes a very little way toward answering it. After its administration, arsenic certainly soon appears in the urine and in the feces and probably is chiefly got rid of by these routes,. It is equally certain that in the body it is not equally distributed: certain tissues hold most of it and others scarcely take it up at all. We have so far only studied the question thoroughly as regards the liver and the spinal cord and find that the drug lodges in the former largely in proportion to the amount placed in the blood and is apparently not taken up by the nervous tissues in any

* Read at the meeting of the Association of American Physicians, Washington, D. C., May, 1922.

recognizable amount. A few preliminary experiments would suggest that the drug also lodges largely in the long bones and in the lungs.

Several observers have found arsenic in the spinal fluid after intravenous administration, but McIntosh and Fildes[1] failed to detect it in the brain. No work has been yet done, as far as the writers are aware, in analyzing the spinal cord after intravenous injection of the drug.

In reviewing the literature regarding experiments with arsenic it seems that the usual test employed has been the Marsh one, which is now obsolete for the quantitative estimation of small amounts of the drug.

The method employed by the writers is a modification of the Gutzeit test as described in the Transactions of the International Congress of Applied Chemistry in 1912. The principle of the test depends on the formation of arsine from arsenic compounds in the presence of nascent hydrogen. Iron as ferric ammonium alum is added to the material to be tested, which causes a steady and regular evolution of hydrogen, although it inhibits the production of arsine. The inhibitory action of the iron is offset by the addition of stannous chloride to the material. The advantage of this method is that for each test a new set of standards is made under exact conditions as to the materials being examined. The lowest amount of arsenic that can be estimated in this way is 0.001 mg., as arsenic trioxid, and the highest is 0.02 mg. From this the percentage of arsenic in any quantity of material can be easily calculated.

The method used for the separation of arsenic from the organic material was as follows. The material to be tested was treated with hydrochloric acid and potassium chlorate. This causes the arsenic present in the material to be ionized into solution. The material is filtered and in the filtrate the arsenic is in solution. The filtrate is then treated by the co-precipitation method. This is done by neutralizing the filtrate with ammonia, and the addition of ammonia until this is 2.5 per cent in excess. Sodium phosphate and magnesia mixture are next added, resulting in a precipitation, the arsenic being thrown down in the precipitate. The precipitate is dissolved by acid and the arsenic further reduced by the addition of potassium iodide.

The following are sources of difficulty and possible error in the determination of small amounts of arsenic:

1. *Reagents.* One of the greatest troubles is the difficulty of obtaining arsenic-free chemicals. Special acid must be procured, as the ordinary so-called chemically-pure acids always contain arsenic. Likewise a special arsenic-free zinc must be used. In

[1] Jour. Am. Med. Assn., April 14, 1917, p. 1147.

all tests where chemicals have a trace of arsenic a control on the reagents must be run through with the test and the amount of arsenic in the control is then subtracted from the reading of the results.

2. *Glassware.* Ordinary glassware usually contains arsenic which is set free when in contact with acids, different amounts at different times. Thus it is impossible to blank glassware. Hard glass, however, is usually arsenic-free. In all our work *pyrex* glassware was used, each piece being tested before being employed.

3. *Filter Paper.* All filter papers at our disposal contained arsenic, some as high as 0.001 mg. per paper, others a mere trace. Fortunately, each paper of a brand held the same amount of arsenic, and this, therefore, could be subtracted from the readings.

4. *Special Precautions.* Needles and glassware must be carefully washed before being used. This is specially necessary when needles have previously been used for the administration of arsenic.

On account of the rather poor results obtained by clinicians in spinal syphilis after intravenous and intrathecal administration of arsenic-containing drugs much controversy has arisen as to whether arsenic has any special effect on the virus of syphilis when in the spinal cord. We have attacked the problem by giving arsenic medication to animals and then analyzing the cord tissues to find if the drug really reached them at all.

On giving a normal rabbit a dose of phenarsenamine proportional to what is given to man no arsenic could be demonstrated in the cord one hour after intravenous injection, although it was very evident in the blood and the liver. This experiment was repeated several times with the same result. Next the dose was increased in a series of animals as much as eight and nine times. The rabbit getting the smallest amount would have a relatively high therapeutic dose while the one receiving the largest amount had sufficient to produce profound degenerative changes in the liver. All the rabbits were killed one hour after the intravenous injection. Fig. 1 is a graph representing the result of these experiments. It will be seen that the amount of arsenic in the blood rises steadily with the dose; that in the liver rises slowly at first, and later very rapidly, but none is shown in the tissues of the spinal cord. The dose in the lowest animals corresponded to 0.8 gm. in a man and in the highest 5.6 gm. in a man.

It is not surprising that no arsenic appears in the spinal cord when one considers the nature of its tissues. McIntosh and Fildes[2] found that the factor governing the passage of dyes into the brain after intravenous injection was their solubility reaction. This, they state, is a peculiar and not a general lipoid one. It corresponds to a solubility in chloroform and in water or perhaps their partition

[2] Loc. cit.

coefficient in these liquids. In all probability the same holds good for the spinal tissues owing to their composition. Thus from a solubility point of view, no arsenic would be expected to lodge in the spinal cord after intravenous injection and this is just what the above experiment shows.

Failing to detect arsenic in the cord after intravenous injection, the writers next tried the intrathecal route. The first problem was, would the arsenic if introduced into the lower part of the spinal canal diffuse upward? The following experiment would suggest at least that it does not do so to any extent. A glass tube

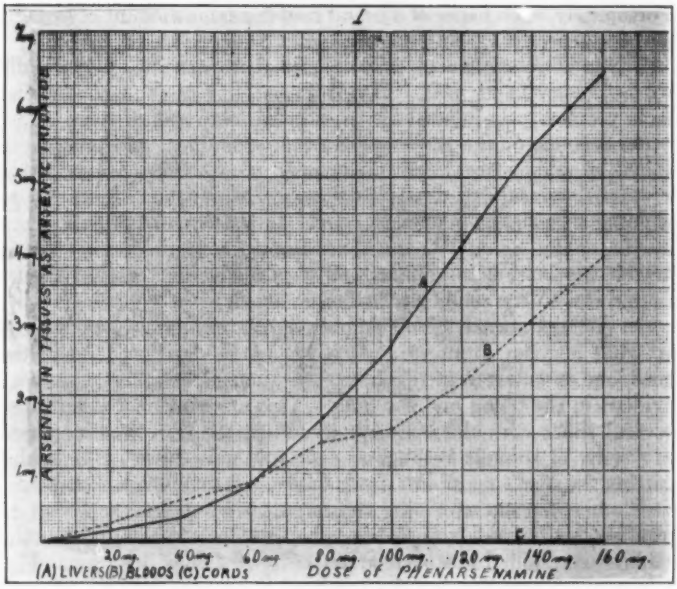

FIG. 1.—Graph.

was filled with 100 cc of water. The vertical column of water measured 53 cm., 10 cc were withdrawn and replaced at the lower end by 10 cc of water containing 1 mg. of arsenious acid. The experiment was repeated using different time intervals, and at the end of the time 10 cc of the fluid were withdrawn from the highest part of the tube and 10 cc from the lowest. Analysis showed that nearly all the arsenic remained in the lowest part of the tube. The experiment was repeated with phenarsenamine with the same result. Fig. 2 shows the results after 6 mg. was injected at the bottom of the tube, and the fluid analyzed twenty-four hours later.

Theoretically it does not seem likely that drugs injected into the

spinal theca should enter the cord tissues as there is normally no circulation in that direction. The writers found that in order to get any arsenic into the cord in this way it was necessary to inject a very large amount. After 1.25 mg. of phenarsenamine in 1 cc of saline solution was injected into the spinal theca arsenic was found in the spinal cord at the end of one hour, the lower part of the cord showing a considerable amount and the upper a mere trace. And this, too, while the spinal canal was more or less horizontal. The results are seen in Fig. 3. It will be seen in this figure that no arsenic appeared in the cord after injection of 18 mg. phenarsenamine intravenously. The amount of arsenic in the control must in all cases be subtracted from the readings.

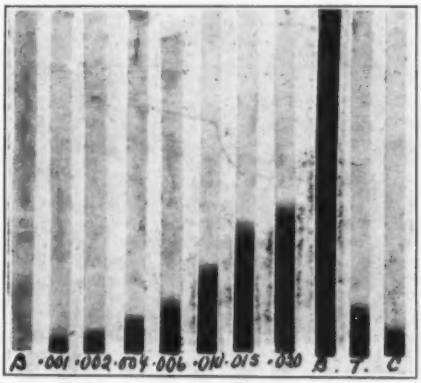

FIG. 2.*—Diffusion experiment, using phenarsenamine. Time twenty-four hours: B, 10 cc from bottom of tube; T, 10 cc from top of tube; C, control of reagents.

In the above experiments it must be remembered that not only was a very large amount of arsenic injected into the theca but that this was done under considerable pressure.

Rabbits receiving sufficient arsenic intrathecally to show in the cord at death if permitted to live all suffered paralysis after the injection. This paralysis seemed to improve somewhat but up to the time that they were killed, one hour later, nothing like complete recovery took place. In order to determine if the paralysis was due to pressure or to the arsenic two rabbits of the same litter were treated as follows: One was given 0.75 cc saline solution intrathecally and the other a similar amount of saline containing 1.25 mg.

* In the illustrations here given the first column is always a blank of the reagents used in the actual test and the next seven show the stains produced by different amounts of arsenic in milligrams as enumerated underneath. The remaining columns show the stains produced by the arsenic in the tissues analyzed, one being always a control of the reagents used in the extraction of arsenic from organic material in a suitable form for analysis.

of phenarsenamine. The animal that received the pure saline showed weakness in the hind limbs but within an hour this had disappeared. The rabbit that received the phenarsenamine intrathecally showed a profound paralysis in the hind quarters. In thirty minutes this had somewhat lessened and the animal was able to draw up the limbs. Two hours later the paralysis was much less but the animal had developed a general tremor. In six hours the animal could hop. Twenty-four hours after the injection profound paralysis had set in, with incontinence of feces. Next day the weakness had reached the fore limbs; the animal was weak and died forty-nine hours after the injection, apparently of paralysis of the respiratory system. This experiment shows that very grave results followed if arsenic gets into the spinal cord in sufficient amounts to be detected by analysis.

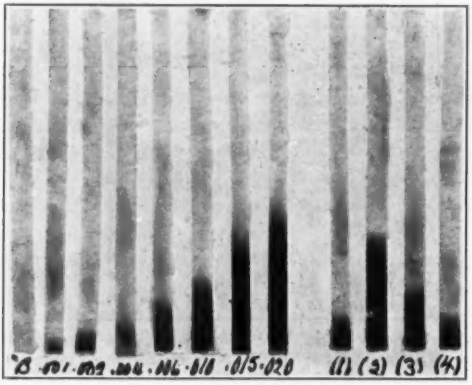

FIG. 3.—Analysis of spinal cords after administration of phenarsenamine: 1, Intravenous injection of 18 mg.; 2, lower half of cord after 1.25 mg. intraspinally; 3, upper portion of same cord; 4, control cord; no arsenic given to animal.

We next tried whether a solution of arsenic in blood serum would induce the deposition of arsenic in the cord. Many experiments were done with serum prepared in the manner proposed by Swift and Ellis. Both cats and rabbits were used in the work, with the same results. Fig. 4 shows the findings in a series of cats. The Swift-Ellis serum used was always prepared from the cat it was afterward given to. In each case the cat was given 75 mg. of phenarsenamine intravenously, an enormous dose when compared to the therapeutic one. An hour later the animal was bled, the blood centrifuged and the blood serum obtained placed in the ice box over night. Then it was diluted to 40 per cent with normal saline, inactivated for a half hour at 57° C. and then used as described. As will be seen from Fig. 4 there was no arsenic

found in any of the cords after the blank of the reagents had been subtracted. It will also be noted that the Swift-Ellis serum showed only a trace of arsenic which of itself would account for the finding of no arsenic in the cords after its intrathecal use. Each of the animals preparatory to our making the serum received a far higher dose of arsenic intravenously than is ever given therapeutically.

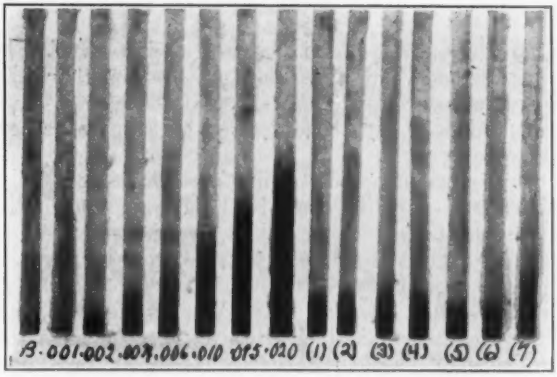

FIG. 4.—Analysis of spinal cords after administration of phenarsenamine and Swift-Ellis serum: 1, Intravenous injection of .25 cc Swift-Ellis serum; 2, intraspinous injection of .25 cc Swift-Ellis serum; 3, no Swift-Ellis serum given (In 1, 2, and 3 cats have had 75 mg. phenarsenamine intravenously); 4, control cord; 5, control of reagents; 6, one cc serum prepared from control cat after Swift-Ellis method only cat received no arsenic; 7, one cc Swift-Ellis serum from cat 2.

When one considers the small amount of arsenic, if any, that reaches the cord after intravenous administration, even when this is supplemented by intrathecal injection next day, it seems unlikely that any possible good effects in the treatment of cerebrospinal syphilis by either the intravenous use of salvarsan or this enhanced by intrathecal injection of arsenic-containing blood serum can be due to the presence of any of the drug in the cord, but must be explained in some other way.

The writers desire to record their gratitude to Professor L. Joslyn Rogers for much skilled advice in regard to the technic here used, and also to Professor V. J. Harding for constant assistance.

Conclusions. 1. When arsenic is injected intravenously little if any of it reaches the central nerve tissues.

2. When it is given in therapeutic doses intrathecally none of it can be detected in the spinal cord.

PNEUMOTHORAX IN TUBERCULOSIS.

By J. J. Singer, M.D.,
(instructor in clinical medicine.)

(From the Department of Internal Medicine, Washington University Medical School.)

It is not the purpose of this paper to go into the literature of the many methods and investigations in pneumothorax, but to merely give a short description of one of the methods used and the various kinds of lung conditions which seem to be benefited by this procedure.

For many years new and startling cures have been foisted on the public, and so positive have been the claims of most of the discoverers that even Congress has investigated certain cures. From many years of experience with the various cures it is conceded that rest and proper diet offer the most in the line of cure.

In discussing the various factors which constitute rest, one must consider pneumothorax in this light. It is my opinion that the beneficial effect of pneumothorax is primarily the rest given to a diseased lung. Conversely, overactivity of the lung during exercise increases the diseased process.

The mechanical factor of rest as produced by pneumothorax—that is, placing the air cushion between the lung and the chest wall—is very simple. As we breathe, air is forced into the lungs through the bronchial tree. The bronchial tube represents the line of least resistance, and thus the air is forced into the alveoli of the lungs (Fig. 1). As the bronchial tubes simply represent the conduction channels of the air, it therefore becomes a relatively simple matter to close the line of conduction by pressure on the lungs. In this condition the tubes in the opposite lung being the line of least resistance, air will then be forced into them and thereby give the desired rest to the diseased lung (Fig. 2).

Pneumothorax Apparatus. This consists of a stand upon which an upright is fastened. On the upright portion a manometer is placed. Two 500 cc bottles are arranged on the base, one upright, *B*, and one inverted, *D*. The height of the upper bottle is adjustable, as seen in the illustration. The upright portion of the instrument contains clips in which various test-tubes for the necessary solutions are kept *K*, also a hand bulb, *L*. The tube *A* connects with a two-way valve *F*, so that the current or pressure can be directed from the bottle *B* or to the manometer through the tube marked *G*. This apparatus is placed in a covered box. The apparatus is portable, its weight being twelve pounds.

The *modus operandi* of the instrument is as follows: By connecting the hand bulb to the upright bottle after disconnect-

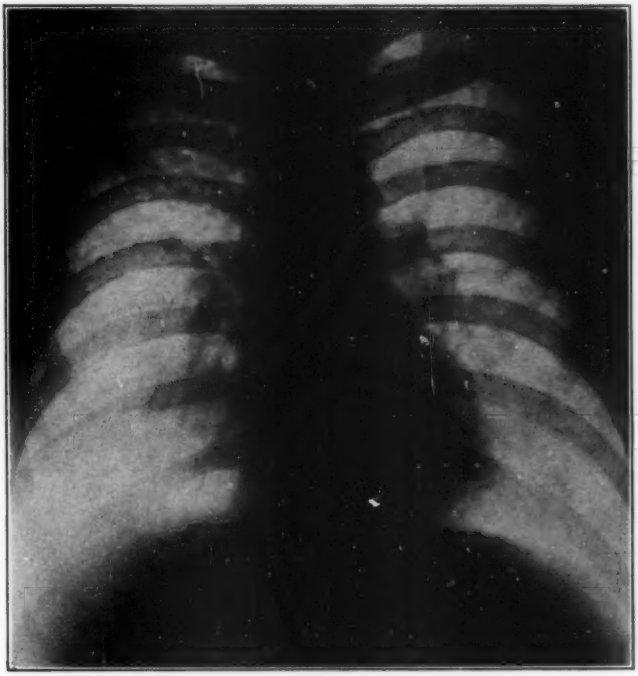

PLATE I.

Shows evidence of tuberculosis in the right upper lung down to the fourth rib. This patient (Mr. W.) had repeated hemorrhages in the month previous to examination. Temperature 101°, with persistent cough. After several pneumothorax injections the condition of the lung is shown in Plate II.

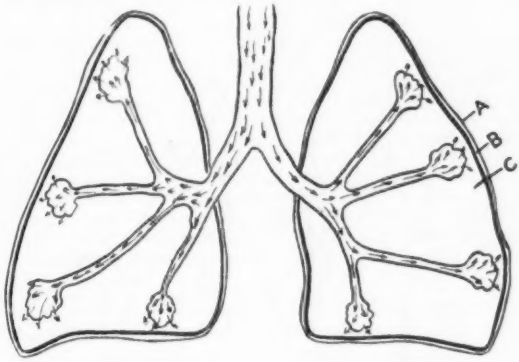

FIG. 1.—A schematic drawing showing the trachea with the bronchial tree and alveoli. *A* represents the parietal pleura, *B* represents the normal pleural cavity and *C* represents the lung. The arrows show the course of the air breathed. Note the equal distribution in both lungs.

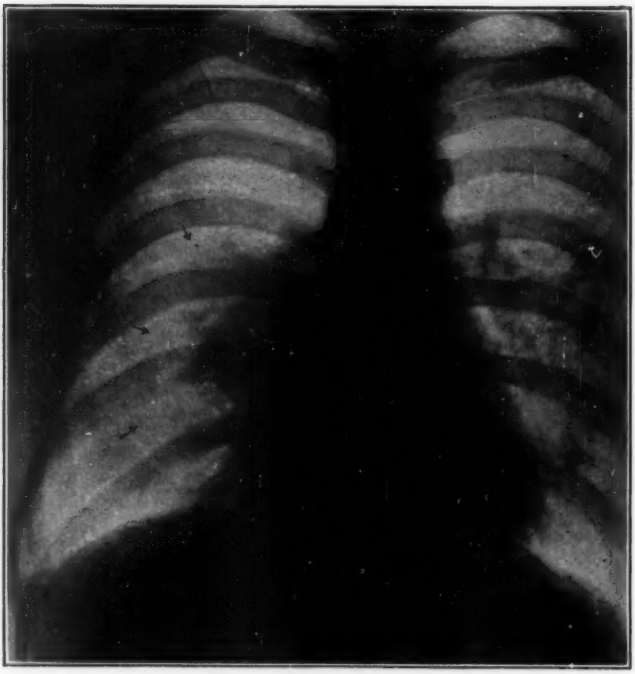

PLATE II.

Note the complete collapse of the lung about the hilus on the right side. There was a complete cessation of hemorrhages from April 9, 1920, as injections up to date. It has been necessary to refill the lung with air every three or four weeks. Note the relative freedom from tuberculous infection in the left lung. This complete compression is not usually seen on account of adhesions which are usually present in most lungs.

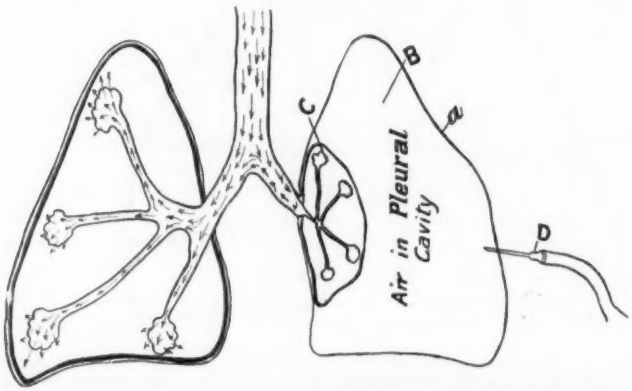

FIG. 2.—A schematic drawing shows how the introduction of air into the pleural cavity *B* compresses the bronchial tree, so that the air currents are directed into the opposite lung. Note the size of the pleural cavity *B* after air is injected. The pressure of the air against the lung closes the bronchial tree of the side.

ing the tube at *A*, air is forced into the same; this forces the water through *C* into the upright bottle *D*. By connecting the tube at *A* and closing the valve at *F* the water will remain in *D:* By opening the valve at *F* the water slowly drips from *D* into *B*. This

PLATE III.

Plate III is the plate of a patient (F. R.) who had tuberculosis in both lungs, and owing to severe and repeated hemorrhages and the hopelessness of her condition it was decided to do a pneumothorax on the side which seemed to be less affected. It will be noted in the second interspace on the left side that there is a dense, dark, annular shadow, and there are also areas of dense fibrosis; the right lung has been partially collapsed, but the adhesion seen between the first and the second rib shows why the complete collapse could not be effected. It is in this class of adhesions that Jacobaeus recommends cauterization through the thoracoscope. We can also note the annular shadow, which is not compressed. These particular shadows have been described as localized pneumothoraces. Formerly this type of shadow was considered by most men as evidence of cavities, but it was noted that the physical signs of cavities did not exist in these cases. (Lawrason Brown.)

forces the air into *B*, through *A*, on through the tube and through the needle *J* and into the chest cavity. The air is filtered through sterile cotton before being admitted into the chest. To register the pressure in the chest, the valve *F* is connected with the manometer, and by noting oscillations as varying negative during inspi-

ration and expiration one will know when the needle is in the pleural cavity. Until one is sure that the needle is in the pleural cavity he should not connect the air in *B* with the needle *J*. During the operation the pleural pressure should be taken from time to time, so that as soon as the positive pressure is noted great care can be used in the introduction of more air, as the adhesions might be torn and hemorrhages occur, and collapse of the patient might result.

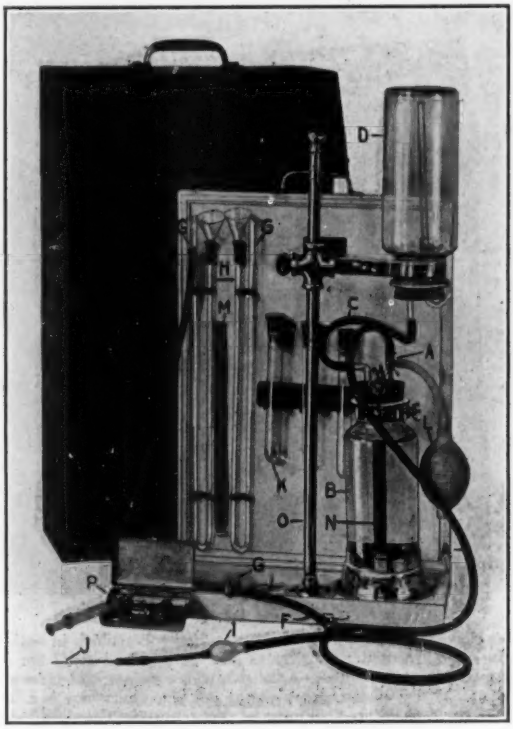

FIG. 3.—This drawing represents the portable pneumothorax apparatus which is used in our work. Its simplicity is such that similar instruments can be made by anyone who possesses any mechanical skill. The outfit shown weighs twelve pounds, and occupies very little space. (See text of the article describing the method of operation.)

The site of injection should be swabbed with tincture of iodin and alcohol. We use novocain, 0.5 per cent, as a local anesthetic on the skin and pleura. The location of the puncture, of course, depends on the physical signs and roentgen findings. When possible the axillary line is used, as there is less muscle and fat tissue at this site.

The first treatment is usually the most severe, as most patients fear the operation and the sensation of pain seems to be most acute at this time. It is very seldom that any untoward symptoms result, except a slight pain in the shoulder of the side treated. This is due to reflex irritation of the pleura. Occasionally patients become dizzy and nauseated. Frequently fluid collects (hydropneumothorax) in the chest cavity, but it is rarely of any importance, although at times it may become infected (pyopneumothorax).

PLATE IV.

Plate IV is that of a patient (M. S.) admitted November 1, 1920. This dense shadow in the chest so obliterated the markings in the lung that it was impossible to tell by physical signs or the roentgen ray whether this was due to fluid or complete consolidation. Thoracentesis done at this time gave dry tap, and a diagnostic pneumothorax was done.

The amount of air injected varies with the pressure recorded. Occasionally 100 cc will register a positive pressure. This is due to the air being injected in a pocket in the pleura. At the next treatment, which should be done in a few days, more air should be injected so that a gradual pressure on the adhesions will result. If this does not occur after several injections it is best to discontinue the treatment.

Jacobaeus[1] recommends the use of an electrocautery needle inserted through a trocar between the ribs to sever the adhesions between the lung and the chest wall. Previous to this operation he inserts an instrument, called the thoracoscope, in between the ribs and finds the adhesions. Occasionally hemorrhages result with fatal results. So far as I know no one in this country uses this method.

PLATE V.

Plate V shows the same patient after several fillings with air; this was taken on December 10, 1920. Note the almost complete collapse of the lung with the cavity between the third and fifth interspace, which was not compressed. One can readily see by comparing Plates IV and V how important the diagnostic pneumothorax is, as without this procedure described no true interpretation of the lung could be made.

However, the time may come when surgery of the chest will be much more safe than it is today and the surgeon will not hesitate to remove the adhesions from the lung, and it may be as simple a matter as removing adhesions within the abdomen.

[1] Beiträge zur Klinik der Tuberculose, 1915, **35**, 137.

PLATE VI.

Plate VI which was taken on the same patient on March 15, 1921, showed evidence of fluid, "hydropneumothorax." The lung is shown partially collapsed, with fluid in the base of the pleural cavity and air above the fluid.

Complication of serous effusion occurs in one-third of the cases.

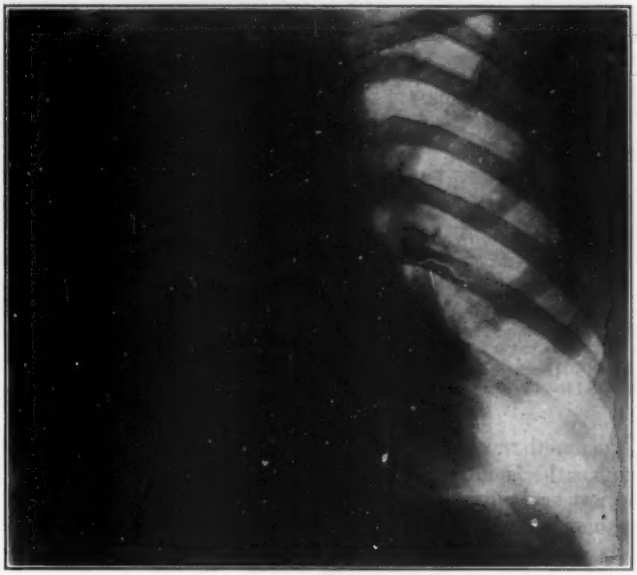

PLATE VII.

Plate VII is that of a patient (R. B.) admitted December 18, 1920. The entire right chest was more or less obliterated by a dense shadow. The physical signs were such that no definite character of his lung can be made out. Comparing this shadow with the one in Plate IV, one sees a striking resemblance. After a diagnostic pneumothorax was done (see Plate VIII) note that the shadow was due to fluid.

The collapse of the lung need not be complete to obtain beneficial results. It is not at all unusual for patients to say they have less cough and that fever is less after the first injection. How much benefit is due to imagination I do not know. However, after more or less collapse most of the patients are improved objectively. The illustrations will show varying degrees of compression in which satisfactory symptomatic results have occurred.

PLATE VIII.

Plate VIII shows the condition of the chest after the introduction of 200 cc of air. The fluid level is easily seen at the junction of the introduced air.

Pneumothorax can be done in the physician's office provided one has the facilities for proper roentgenological examinations and the proper facilities for sterilization. Most patients can take the pneumothorax sitting in a chair or on a stool, and are able to leave within a few minutes after the operation. The entire treatment can usually be done in ten minutes.

Spontaneous Pneumothorax. The danger of spontaneous pneumothorax is great, as the sudden filling up of the pleural cavity

with air through a tear in the lung compresses the lung and pushes the mediastinum with its vessels into the opposite chest cavity. The sudden pressure occurs before the compensatory mechanism of the body can adjust itself to this condition. When a spontaneous pneumothorax occurs the patients are usually in a state of body collapse—marked dyspnea, cold, clammy skin, and occasionally the patient dies. Spontaneous pneumothorax occurs in tuberculosis fairly frequently, so that compression gradually done will

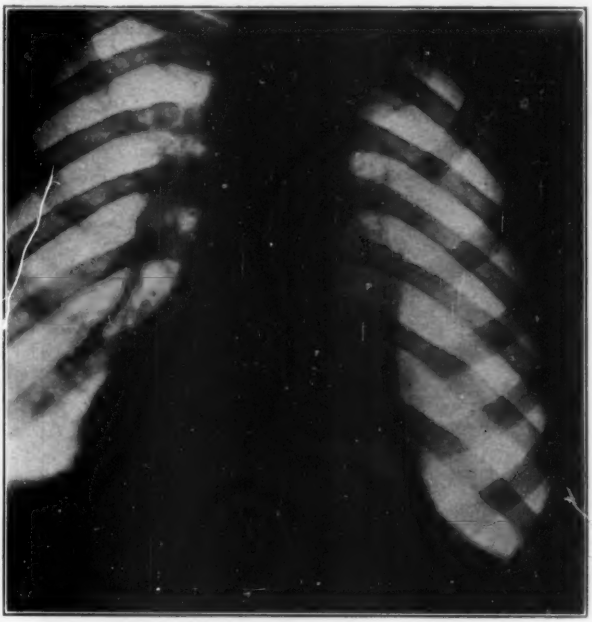

PLATE IX.

Plate IX shows the chest after removal of practically all of the fluid. It will be noticed that the lung had not reëxpanded. This condition is due to the dense adhesion which extends vertically through the chest; this condition will always remain as a chronic pyopneumothorax unless a radical operation is done, in which the ribs are removed and the adhesion severed. This was not done in this case because it proved to be tuberculosis.

prevent in many instances a spontaneous collapse. By reversing the pneumothorax outfit described in this paper and connecting the chest cavity through the needle *J* to the bottle *D*, which is filled with water, the air is extracted from the pleural cavity until a normal manometer pressure is noted.

Diagnostic Pneumothorax. It has been suggested by Fishberg[2] that the diagnostic pneumothorax will bring certain extrapulmonary

[2] Jour. Am. Med. Assn., 1921, **76**, 581.

masses into better view. "In about 50 per cent of cases of malignancy of the lung, pleural effusion" (serous, sanguineous or purulent) takes place and diagnosis is then rendered more difficult. When this takes place the entire one-half of the affected side of the chest is obscured in the roentgen plate by a dense homogeneous shadow and the usual roentgenographic report is pleural effusion. By the removal of several hundred cubic centimeters of this fluid and injecting nitrogen or air the extrapulmonary condition can be readily noted.

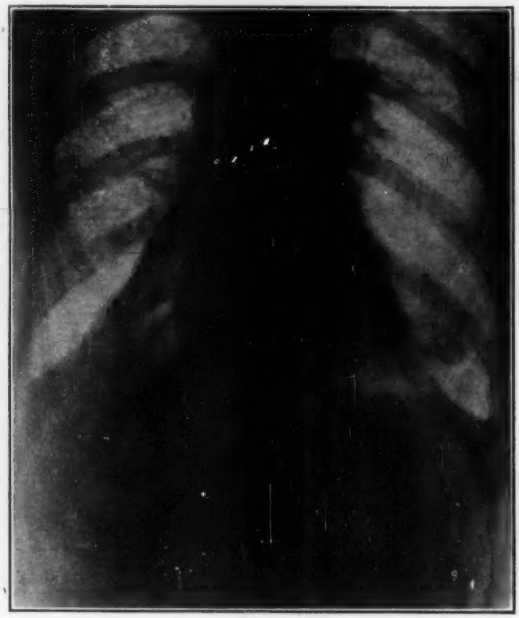

PLATE X.

Plate X is of a patient (A. S.) taken December 17, 1920. It will be noted that the dense shadow extends from the hilus on the right side downward and blending with the diaphragm, and it is three-quarter inches wide. The physical signs and history warrant a diagnosis of bronchiectasis. The patient would bring up two or three times a day from eight to twelve ounces of purulent sputum. This condition followed an attack of influenza. For two years she was unable to lie down in bed on account of severe paroxysms of coughing and the sensation of smothering.

In using the diagnostic pneumothorax we find that when fluid is present in the pleural cavity only one or two operations are necessary to determine lung detail.

Pneumothorax in Other Chest Diseases. Pneumothorax is indicated in severe bronchiectasis, abscess of the lung and empyema emptying into a bronchus.

Severe bronchiectasis may be benefited by pneumothorax. It is simply marvellous to see the improvement following the collapse of the lung. Patients who have been bringing up purulent sputum from four ounces to a pint, and who have found it impossible to lie down in bed, after the second injection will have little or no sputum and be able to lie down in any position. Occasionally, however, in bronchiectasis we have very dense adhesions which

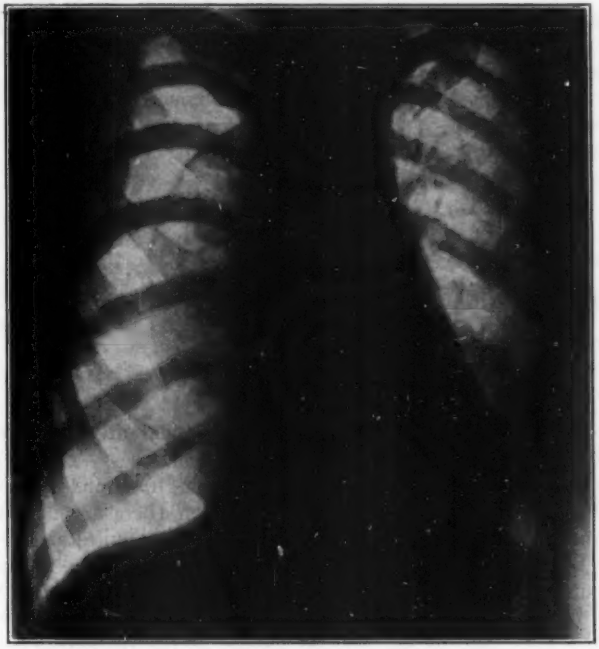

PLATE XI.

Plate of the same patient taken November 13, 1921, shows a collapse of the lung following artificial pneumothorax. In this case compression was done on account of the severe hemorrhages which occurred two weeks previous to the introduction of artificial pneumothorax. One can note in the base of the lung the collapse of the bronchiectatic area. Since the operation patient has had no hemorrhages, and is able to lie down without coughing and bringing up only an ounce or two of purulent sputum daily. Apparently the bronchiectatic cavities are all collapsed.

prevent collapse of the lung. In these cases surgery is indicated. The procedure used in bronchiectasis is the same as described before in the early part of this paper.

In cases of abscess of the lung, when patients are bringing up purulent sputum and when there is a connection between the abscess cavity and a bronchus, good results may be obtained in this condition.

Empyema with bronchial fistula, especially in tuberculosis, can be treated by this method. The pressure of the air forced into the cavity will force the fluid through the bronchus, and this can then be expectorated.

Conclusion. 1. The most suitable cases are one-sided tuberculosis or moderately advanced cases with proper compensatory lung tissue.

2. Cases with hemorrhages are especially benefited by pneumothorax.

3. Bronchiectasis, lung abscess and tuberculous empyema are frequently very much improved.

4. As a diagnostic measure of the lung condition it offers considerable.

I wish to thank Dr. George Dock and Dr. Albert Taussig for their kindness in supervising this work.

THE SURGICAL NEUROSES OF THE THYROID GLAND.[1]

By John Rogers, M.D.,
NEW YORK.

The conditions which result from an apparently overacting thyroid gland were formerly classified as neuroses. These disorders can be defined as abnormalities in the functions of one or more parts of the nervous system for which there are no corresponding demonstrable nerve lesions. The manifestations of hyperthyroidism are of this character and should be designated as neuroses because that terminology helps to direct attention not only to the probable locality and manner in which the thyroid product acts, but to the general nature of the disturbance. It seems to be traceable to certain alveoli which differ from those of the normal thyroid, and if the duration and intensity of the process is sufficient morphologic changes occur in other organs. To prevent these, and to relieve or cure the antecedent neuroses, experience has proved the necessity of surgery. But operative treatment alone should be regarded as fulfilling only a small part of the indications, for these neuroses are essentially the same as all others, that is, dependent in all probability upon some preceding defect or deficiency in the nervous biochemistry. Either the nerve tissue itself is "weak," which means that the nutritional chemistry of the nerve elements is not as sound and vigorous as it should be, or else that there is a defect or deficiency in the metabolic processes

[1] Read before the Surgical Section of the Buffalo Academy of Medicine, March 1, 1922, and the Philadelphia County Medical Society, May 11, 1922.

of the viscera upon which the nervous nutrition depends. The deficiency may be a congenital and inherent, or an acquired error, or it may be secondary and related to the so-called vitamin or deficiency diseases with which some of the thyroid neuroses present many analogies. Certainly the administration of minute doses of thyroid material or of iodin can occasionally produce remarkable results. Thus, many of these hyperthyroid neuroses are strongly suggestive of some primary weakness or defect in the nutrition, especially of the involuntary nervous system, and of changes in the thyroid which are secondary. That is, many individuals seem to possess "weak nerves," and conditions which require their active functionation necessitate a corresponding thyroid activity, and this organ, of evident importance for the nervous nutrition, then fails or "overacts." These cases are generally characterized by the presence of neuroses which precede, and later accompany, the recognizable hyperthyroid symptoms, and usually show only a small or insignificant "goiter."

Others, and they probably constitute the majority of the hyperthyroid cases, seem to originate not in "weak nerves" but in a "weak" thyroid, and this has a very close relationship to the gland's ability to obtain or to metabolize iodin. A deficiency of this element in the ingesta seems to be a common cause of "goiter," or, more correctly speaking, of simple hypertrophy which, certainly in animals, may be accompanied by more or less evident signs of hypothyroidism. As the feeding of iodin to these animals is followed by a disappearance of all symptoms, the hypertrophy seems to represent an attempt to compensate or to supply some deficiency. In man a lack of iodin in the ingesta is not so easily demonstrable, and there also seem to be other variables. For the simple hypertrophy of the thyroid, which is so common in growing children, especially during adolescence, does not always subside with the administration of iodin. Indeed, too large or too frequently repeated dosage may even be followed by increased hypertrophy or by the development of adenomatous or cystic changes.

The latest determinations place the iodin content of the normal human thyroid at 0.5 mg. per gram of fresh gland substance.[2] The hyperthyroid gland seems unable to hold this amount, and the severity of the symptoms is more or less proportionate to the thyroid's lack of iodin. Feeding this element generally increases the disturbance, though it may prove inert or temporarily beneficial. In the latter case the gland usually first enlarges and gives a sensation of constriction or pressure, and if then the iodin is continued there follows an exacerbation of the process which may be dangerous. Rarely a very small amount of iodin, especially if combined with

[2] Zunz: Arch. Int. Physiol., 1921, **16**, 288.

adrenal feeding, as will be described later, may prove curative. That is, there may be an abundance of available iodin, but the thyroid cannot without assistance from other organs metabolize it. The gland is not independent and its unaided functional capacity is limited.

Clinical observations are not entirely trustworthy but they seem to show that the great majority of the hyperthyroid disturbances begin rather gradually and run a more or less recognizable course. There is the not inconsiderable group which, as stated above, apparently start with "weak nerves" or ill-defined neuroses, with an irritable and then a constantly rapid pulse. The enlargement of the thyroid is then and thereafter slight or inconspicuous. These cases generally present a much less favorable surgical prognosis than the other more common group, which seem to start with a "weak" thyroid. The latter, as it gives the first noticeable symptom, is apparently the primary lesion. In these cases there is an initial simple hypertrophy which can be reasonably regarded as an attempt to compensate or to supply demands which exceed the gland's functional capacity. These demands apparently emanate from every organ, and especially from the nervous system, and in each seem to pertain to the chemistry which promotes that organ's functional activity. For in recognizable hypothyroidism the chief symptoms may be of deficient functionation in almost any part of the body, and any or all of these symptoms can often be relieved by the right kind of thyroid feeding. Then, after the appearance of the hypertrophy, unusual or excessive functionation in other organs or groups of organs is regularly followed by increase in the size of the "goiter," and cessation of this activity by its shrinkage.

The gland when overactive is well known to accelerate metabolism and to be intimately connected with oxidation. It is not the only factor in this process, but its importance is shown by Kocher's "cachexia strumipriva," which is irremediable unless Kendall's thyroxin should prove efficient. Because of these evident relationships the chief if not the only function of the thyroid apparently is the promotion through the process of oxidation of the organism's chemical reactions. Or more briefly and less accurately, the gland's purpose seems to be the "production of energy." To fulfil this duty the organ must have available a certain minimum amount of iodin, and it must possess a certain minimum amount of epithelium which is capable of functioning. The functional capacity of the epithelium, and the factors which regulate its nutrition and so its functional capacity, or the multiplication or atrophy of its epithelium, can only be surmised. But they evidently are variable and even more important than the circulating iodin.

The conditions, then, under which the first signs of the hyper-

thyroid neuroses develop are almost always those requiring an excessive expenditure of one or another kind of energy. This may be to resist acute or chronic infections, or to endure pregnancy and labor, or to sustain muscular exertion, or most often to withstand an unfavorable environment. An inefficient thyroid, then, responds to those demands for its "production of energy" by simple hypertrophy. Coincident with, or following, this evidence of an attempt at compensation there are usually pallor, more or less headache and lassitude or weariness, and signs of deficient gastrointestinal activity. These are the signs of ordinary fatigue and cannot be differentiated from that common condition except by the presence of the "goiter." When the goiter is perceptible the symptoms are generally accepted as those of hypothyroidism. If the causes which induce the excessive (and this varies with each individual) expenditure of energy persist, the preceding quiet pulse-rate becomes "irritable" and then constantly rapid, and with this phenomenon there occur the usual increased, or perhaps "unchecked," vasomotor, cutaneous, respiratory and gastrointestinal activity or evidences of hyperthyroidism. The exophthalmos, if it occurs, generally appears last. Its origin is unknown, but this symptom adds materially to the gravity of the prognosis.

An unfavorable environment is one of the most common causes for provoking expenditure of energy, and many individuals, in all probability, by avoiding this environment because of the symptoms it excites, seem to have their disturbance arrested midway between hypothyroidism and typical hyperthyroidism. These cases form the rather large group which give the so-called "mixed" or coexisting signs of both hypo- and hyperthyroidism. If it can be accepted that the disease starts in an initial simple hypertrophy, apparently to compensate for an expenditure of more energy than the normal gland can supply, and passes through a hypo and then a mixed hypo and hyper stage and finally into typical hyperthyroidism, then the gland should be treated at least with conservatism. The hyperthyroid condition in following this course gives strong evidence of originating in a "weak" thyroid which "overacts" not because of a primary and vicious functionation, but because the gland's epithelium, under "strain" or demands which are excessive, fails in its power to metabolize iodin.

The initial simple hypertrophy may at any time, especially if the conditions are those which require much expenditure of energy, be complicated by the development of a cyst, or cystadenoma, or a "toxic adenoma." Apparently, the demand upon the thyroid for functionation is accompanied by congestion which may obstruct an alveolus and lead to a "retention" cyst or cause an intraglandular hemorrhage with a reactive and often encapsulated epithelial proliferation. The epithelium in and immediately around the damaged area seems to have less than the normal functional capacity, and

its iodin metabolism, therefore, becomes faulty. The resultant general symptoms are the same as those of ordinary hyperthyroidism, except that these cases less often develop the highest metabolism tests and less often show marked exophthalmos. But some, especially the multiple toxic adenomata, may show all of these signs.

The symptoms of the typical hyperthyroid neuroses are traceable chiefly to abnormal or "unchecked" activity in the functions performed by the autonomic or parasympathetic nerves. This group might be more generally appreciated if it were designated by the name of its most prominent member, or as the vagus system. The flushed and moist skin, the usually low blood-pressure, the overacting rather than the merely rapid heart, the lacrimation and salivation, the abnormal hunger and the frequent bowel movements, are all referable to these nerves. That is, the accepted symptoms of an overactive thyroid are those of overactivity in the autonomic or vagus, and not in the sympathetic system. A great many cases, however, show only a simple tachycardia and practically nothing else except a thyroid enlargement and some vague "nervousness." These symptoms certainly may indicate the existence of a hyperthyroidism, but they do not necessarily prove that the thyroid product stimulates or acts through or upon the cardioaccelerator, or at least one of the sympathetic nerves, and much less all of the group.

While testing the effects upon dogs of various derivatives of the thyroid it was found that noncoagulable extracts excite immediate and definite responses. The most active of these preparations seemed to be a slightly hydrolyzed aqueous extract which was designated as the thyroid "residue" because it consisted of what remained, after the removal by boiling in dilute acid and alkali, of all coagulable material. Another extract made with 95 per cent alcohol, then evaporating the alcohol and adding water, was nearly but not quite as active. Each was standardized to contain 0.05 mg. of iodin per cc. The responses which these noncoagulable extracts provoked were vasodilatation, apparently through stimulation of the vasodilator nerve terminals, an increase in the salivary flow and a vigorous stimulation of the flow of the gastric and pancreatic secretions.[3] There was also some stimulation of the gastric and intestinal peristalsis. A dose of atropin which, of course, paralyzes the terminals of the vagus, prevented or stopped this stimulation. After section of the vagus just above the diaphragm and degeneration of its peripheral fibers, the injection of the noncoagulable thyroid extracts produced little or no effect. Thus, at least in the case of the stomach and pancreas, the noncoagulable extracts of the thyroid apparently act through and upon the terminal

[3] Am. Jour. Physiol., 1916, **39**, 345; Ibid., 1919, **48**, 79.

filaments of the vagus. They may also produce more or less diuresis. In the kymograph tracings there was no thyroid derivative which would cause any appreciable degree of tachycardia. This seems to mean that the product of the thyroid does not stimulate the cardioaccelerator nerve nor, for that matter, any other part of the sympathetic system.

These particular nerve endings are, of course, activated or stimulated by epinephrin; therefore, experiments were next carried out with derivatives of the adrenal gland (all of which contain at least traces of epinephrin), and it was found that a slightly hydrolyzed aqueous extract made like that from the thyroid and designated as the adrenal "residue" (because it contained all that remained after removal of the coagulable materials) prevented or stopped the stimulation excited by the noncoagulable derivatives of the thyroid. The coagulable derivatives of the adrenal gland, like the nucleoprotein material, contain only faint traces of epinephrin, while the noncoagulable are quite rich in this substance; they all excite vasoconstriction or raise the blood-pressure in proportion to their epinephrin content. They all also stop or prevent the stimulation by the noncoagulable thyroid derivatives of the stomach and pancreas. But these effects, though apparently brought about by direct excitation of the functions believed to be performed by the terminal filaments of the sympathetic are not those of epinephrin. At least, a dose of adrenalin which is equivalent to the epinephrin content of the adrenal nucleoprotein material, or to the noncoagulable derivatives of the entire gland, shows comparatively slight inhibitory powers. That is, the supposed active principle of the adrenal gland is not nearly as vigorous an antagonist of the thyroid derivatives as are at least some of the materials which can be extracted from the whole adrenal gland. Because the adrenal nucleoproteins and the slightly hydrolyzed aqueous extract (adrenal "residue") produced so marked an inhibition of the gastrointestinal functionation, apparently through stimulation of the sympathetic nerves, their effects were next tested, in comparison with commercial adrenalin, upon the iodin content of the dog's thyroid. The noncoagulable extracts given hypodermically are followed by severe and sometimes fatal reactions. Therefore, crystals of commercial adrenalin and the adrenal nucleoprotein material and the adrenal residue were fed over a period of six weeks by mouth. The dosage of each was standardized by its epinephrin content. One thyroid lobe was removed from each animal at the beginning of the experiment and the other at the close. It was then found that the thyroid lobe in the dogs which were fed adrenalin showed, as compared with the control animals, a practically negligible gain in iodin. Those fed the adrenal nucleoprotein material showed an average gain

of about 50 per cent while those fed the adrenal residue gained about 75 per cent.[4]

It is well known, as stated previously, that in cases of excessive activity of the thyroid the gland contains per gram of gland substance less than the normal amount of iodin, and the greater the loss in iodin the more severe seem to be the symptoms. Therefore, because the feeding of derivatives of the *entire* adrenal gland results in a gain in the thyroid's iodin, it is reasonable to believe in some inhibitory effect of the adrenals upon the thyroid, probably through the intermediation of the latter's sympathetic nerve supply.

The impulses discharged from the sympathetic, as determined by electrical and chemical tests, produce vasoconstriction and, in general, inhibition of gastrointestinal activity. Those from the autonomic or vagus system, on the other hand, excite, as a rule, vasodilatation and increased gastroenteric functionation. As the thyroid product, both clinically and experimentally, seems to have a selective and stimulating affinity for the autonomic or vagus terminals, its part in the production of chemical energy can be briefly described as that of "drive." The adrenal product, by its corresponding effect upon the opposing or sympathetic terminals, can then be supposed, by its inhibition of functional activity, presumably through each organ's metabolism, to act as the opposing automatic "check." Hence, theoretically and because of the effects of adrenal feeding upon the thyroid's iodin content, any excess of thyroid activity "drives" the adrenals into activity, probably through their vagus nerve supply, and then the adrenal product returns in the circulation and, probably through the sympathetic terminals, automatically "checks" the thyroid.

Any break in this chain should lead to the development of a vicious circle. Its most vulnerable link ought to be in the terminals of the vagus, or sympathetic, nerves. It is presumable that either the latter or the vagus (autonomic) endings may have their functions interrupted or destroyed by bacterial or other poisons or, as clinically seems common, by fatigue. In the experimental fatigue of voluntary muscles which can be induced by electrical stimulation of their nerve supply, the first effects are those of failing vigor in the contractions due to failure in the function of the nerve ending. When this failure becomes marked the injection into the circulation of noncoagulable derivatives of the thyroid or adrenal glands quickly restores the muscular vigor. If, however, the fatigue is continued until there is no contraction, that is until the function of the nerve ending is destroyed, then the thyroid and adrenal extracts are without effect.[5]

These findings seem to have some significance in the origin of

[4] Am. Jour. Physiol., 1918, **45**, 97. [5] Ibid.

the thyroid neuroses and their treatment, for fatigue should be capable of interrupting the functions, also, of the involuntary nerve terminals, and if the sympathetic supply of the thyroid fails the gland should lose its automatic "check" and then ought to overact. Clinically, however, when fatigue appears to originate the disturbance, at the outset it seems to affect both the vagus "drive" and the sympathetic "check." The accompanying symptoms are those called hypothyroidism. Later, with a continuation or intensification of the fatigue, the sympathetic becomes conceivably more intensely affected, and the ultimate result is lack of check upon the gland and hyperthyroidism. Furthermore, the fatigue experiments mentioned above suggest that organ therapy can be helpful only when the involuntary nerve terminals are capable of at least some functionation; hence, also, the need of rest.

In the differential diagnosis of the thyroid neuroses an evident excess of activity or of "drive" in all or a majority of organs indicates, in the presence of at least a perceptible "goiter," an excess of thyroid product or hyperthyroidism and a lack of drive the opposite condition. We know nothing of a corresponding hypo- or hyperadrenalism. Nevertheless an excess of drive can theoretically mean only a deficiency of the normal check, which may be in the sympathetic and not in the adrenal portion of the chromaffin system.

But in what seems to be the intermediate stages of the disease, or the so-called mixed hypo- and hyperthyroid disturbances, when the hyper symptoms are beginning and advancing from, or perhaps receding into, the primary failure, it is necessary to study the history and the general nutrition and then judge whether more organs are overacting than underacting. If there is only a tachycardia and "nervousness" without any flushed, moist skin and evidence of gastrointestinal activity, the signs of lack of drive predominate over those of its excess, and the condition is one more of hypo- than hyperthyroidism. Just what this means cannot at present be definitely stated, and there is no mechanical test which alone is conclusive. The calorimeter, in my experience, is often more useful in these doubtful cases for proving the existence of hypo- rather than hyperthyroidism, for it not infrequently shows a metabolism which is even 20 per cent or 30 per cent above normal, yet this may be promptly reduced by the *right kind* of thyroid feeding. In the absence of any better explanation it can be imagined that the "mixed" symptoms are traceable not so much to a failure of inhibition in the thyroid as to a failure in varying degrees and in different organs of the sympathetic "check" mechanism with a presumable increase in their metabolism which should be reflected in the calorimeter. There is a general belief, however, that the product of the hyperthyroid gland may vary in both quantity and quality. An alteration in the quality of the

thyroid secretion might then stimulate some and not all parts of the autonomic system; or it might lead to an imperfect adrenal product (as the thyroid seems to be needed by all organs) and this to imperfect inhibition, which would then be expressed as "overactivity" or imperfect balance in some other viscera. In whatever way the complicated disturbance may be interpreted the fact remains that not infrequently in the early or mild or atypical cases of apparent hyperthyroidism the "feeding" of some thyroid derivative will relieve or cure and not intensify the condition. As the administration of iodin may rarely accomplish the same result, there are thus some reasons for believing in a poor quality rather than a mere excess of quantity of secretion.

The materials commonly available for thyroid feeding are prepared by different methods of desiccation of the whole gland, and lately there have been added the nucleoprotein substance which can be extracted from the fresh organ and also an alcoholic extract and a slightly hydrolyzed aqueous extract spoken of previously as the thyroid "residue." As there seemed to be great variations in the clinical reactions of patients to these different preparations our laboratory recently tested the effects upon three groups of dogs of the products of several of the best-known manufacturers. The first group consisted of normal animals, the second were thyroidectomized, and the third, to denervate the organ, had the gland transplanted into the spleen, where, at the close of the experiment, it was later demonstrable. The dosage of thyroid material was standardized so that each animal received by mouth daily an amount which contained approximately 2 mg. of iodin. After feeding one preparation of the entire desiccated gland for a few days the urine of all the dogs, especially those which had been thyroidectomized, showed the presence of glucose. Feeding the similar product of another manufacturer was followed by the appearance of albumin in the urine of the thyroidectomized dogs and in those which had the thyroid transplanted into the spleen. Still another desiccated product caused albumin in the urine only of the dogs with the spleen transplant, or both sugar and albumin. That is, all of the desiccated products regularly caused gross changes in the urine of the thyroidectomized dogs, or in those with a presumably denervated thyroid, and one product seemed to cause albuminuria even in the normal dogs. On the other hand, the preparations like the nucleoprotein material and the thyroid residue made from fresh glands showed no gross ill effects. Hence, as dogs are very tolerant of thyroid feeding it is presumable that a cautious therapeutic test for the existence of hyperthyroidism by the oral administration of the *usual dried gland substance*, though much more harmless than the hypodermic administration of adrenalin, would at least not be positive. But the derivatives like the thyroid nucleoprotein material, which are made from the

fresh gland, seem to be free of toxic effects in animals, and clinically in the border-line cases will often relieve and not intensify the "mixed" symptoms.

When an apparently hyperthyroid condition can be improved or slowly cured by feeding a more or less "nontoxic" thyroid derivative, there is no proof that the original diagnosis was wrong. It is only probable that the popular conception of the disease is wrong. The product of the thyroid epithelium is apparently not excreted, but in some disintegrated form returns to its source and is there recombined. If the epithelium is "weak," it may not be able to recombine a badly disintegrated product, but might be able to utilize a material which is nearer to the normal. The ingestion in comparatively minute amounts of some "nontoxic" thyroid derivative could not materially increase in the circulation the quantity of the pathological thyroid product and might act toward the thyroid epithelium like a specific predigested food.

The tachycardia, which is so constant and characteristic in hyperthyroidism, because of its relationship to the cardioaccelerator nerve, seems to have given origin to the prevailing and apparently erroneous belief that the thyroid acts through or upon the sympathetic nerves. As stated previously, there is no derivative of the thyroid which, experimentally and within the usual laboratory period of two or three hours, will excite this symptom. It only occurs after a rather prolonged treatment with thyroid feeding, and then is apparently an accompaniment of the generally increased metabolism. It may signify an increased metabolism of the cardiac musculature, but evidently is not due to direct stimulation of the cardioaccelerator nerve by the thyroid product.

The peculiar disturbance excited in the doubtful or mixed hypo- and hyperthyroid cases by the injection of adrenalin is of unknown significance. It proves nothing. Because the evidence points toward some primary failure in the thyroid, it would be far more reasonable and much less injurious in guessing at which extreme predominates, to administer some nontoxic derivative of the thyroid. If then, in spite of every attempt to relieve the needs for the production of energy, the signs of too much "drive" upon the viscera persist and are not relieved or are aggravated by cautious thyroid feeding, there is need of surgery.

As stated previously, the ultimate cause of the hyperthyroid neuroses seems to be traceable to certain pathologic alveoli in the diseased gland, for if this abnormal tissue can all be removed, as it can be in some encapsulated "toxic adenomata," the manifestations of hyperthyroidism quickly subside. If it cannot all be removed the immediate relief seems to be more or less in proportion to the amount excised. But to obtain this kind of a result the diseased part of the thyroid must be excised before the neuroses have produced at least pronounced changes in the viscera.

The location and extent of the hyperplasia can only be estimated by the consistency and contour of the gland and by the comparative size and apparent vascularity of the two lobes and the isthmus. For surgical purposes these observations can be expressed diagrammatically as representing three types of hyperthyroid glands, although each is capable of transformation into any of the others.

1. The symmetrically enlarged thyroid of even consistency, vascularity and contour throughout the entire organ. This gland contains, presumably, the hyperplastic tissue equally distributed in all parts and is usually accompanied by the signs of typical hyperthyroidism, and often the worst forms of exophthalmic goiter.

2. The asymmetrically enlarged thyroid in which one lobe is greater in size than the other and generally more dense and vascular, and thus can be more or less surely presumed to contain most, if not all, of the hyperplastic tissue, for the latter contains less colloid and more cells and bloodvessels than the normal tissue. The accompanying neuroses in this type of hyperthyroid gland are usually less severe than in the first, and the exophthalmos may be only perceptible on the side of the enlarged lobe.

3. The thyroid of the "toxic adenoma" type. This gland may be slightly or considerably enlarged, but contains an evidently circumscribed tumor. The accompanying neuroses are usually less severe than in either of the two preceding types of hyperthyroid glands, and are seldom accompanied by exophthalmos. But it is possible for a nontoxic adenoma, or one containing no hyperplasia, to occur in a hyperplastic thyroid which may even be not noticeably enlarged. Furthermore, a comparatively normal thyroid containing a single toxic adenoma can develop, usually under conditions which force the patient to expend much energy, other toxic adenomata, and in addition hyperplasia in the intervening, comparatively normal tissue.

That is, almost any of these three types of thyroid, which seem to represent the initial changes in the gland, can alter into any other and be accompanied by any or all of the hyperthyroid neuroses or symptoms and by the subsequent visceral lesions.

Some if not all of the toxic adenomata seem to originate in a congestion, presumably to promote functionation, and then there occurs a localized hemorrhage. Others apparently begin like a retention cyst. These peculiar alveoli, with their thickened epithelium, seem, of course, to represent a multiplication of the secreting structure of the thyroid with a corresponding increase in the gland's functional activity. Occasionally, and that, too, without any treatment, the hyperplastic alveoli are evidently capable, though slowly, of returning to the normal. The recovery, however, is more frequent after cutting down the circulation by

the ligation of one or more of the superior or inferior thyroid vessels. Hence it is reasonable to believe that the chief stimuli which cause the gland to "overact" reach it through the blood. The same inference can be drawn from the congestion of the organ, which is evident during exacerbations of hyperthyroidism. These surgical aspects of the diseased gland can be readily understood from the accompanying rough diagrams. (Figs. 1, 2, 3).

To be reasonably sure of operative success all, or the major part of the hyperplastic alveoli, must be excised. This is comparatively simple in the second and third types of diseased gland. The

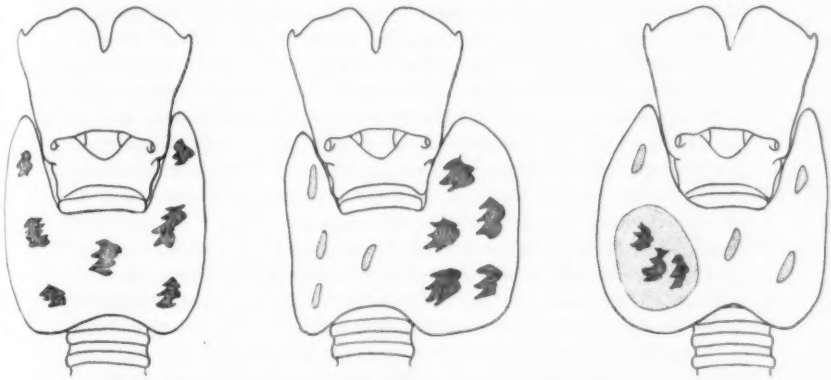

FIG. 1 FIG. 2 FIG. 3

FIG. 1.—The symmetrically enlarged thyroid of even consistency, contour and vascularity. The hyperplastic alveoli are presumably distributed throughout all parts of the gland. Ligation of the four chief vessels is the safest and best operation.

FIG. 2.—Asymmetrically enlarged thyroid. Excision of all or the greater part of the diseased alveoli yields the best surgical result. But relapse or recurrence of hyperthyroidism must be constantly kept in mind and prevented by the right kind of thyroid feeding.

FIG. 3.—Thyroid of the toxic adenoma type. The diseased and generally encapsulated alveoli should be treated by enucleation of the tumors and by ligation of the two superior vessels. There should be no extensive resection of simply hypertrophied tissue. Normal alveoli are represented by the oval shaded patches in the thyroid; hyperplastic alveoli by the darker shaded patches with irregular outline.

removal of the lobe which apparently contains all or most of the pathologic tissue, or the enucleation of a toxic adenoma, fulfils these surgical indications. But it is always wise at the same time to tie both superior vessels, if only because of the unavoidable uncertainty as regards the extent of the hyperplasia. When, however, the goiter is like Type 1, that is, when there is reason to believe the hyperplasia is evenly distributed throughout all parts of the entire organ, the problem is much less simple. The common procedure is to excise four-fifths or five-sixths of the gland or to leave an amount which is more or less equivalent in size to that of

the normal organ. This is probably unwise, as the prognosis for the operative result is uncertain, or at least more uncertain than it should be. In the hands of the average surgeon there is, in the first place, grave danger of the acute postoperative toxemia; and it is worth noting in considering the gland's pathologic physiology, that the greater the amount of the *uniformly* hyperplastic thyroid which is removed the greater seems to be the danger of this violent toxemia. If a considerable amount of diseased tissue remains, the remote result may be bad but there is less risk of an immediate fatality. In the next place, whether little or much hyperplastic tissue remains, to restore health this must ultimately become normal. If it does become normal there must also apparently be enough of the gland to supply the required amount of "drive" or the hyperthyroidism will recur. There seems to be great variations in the amount of thyroid which different individuals require. To meet these uncertainties in the first type of hyperplastic gland, or that in which the diseased alveoli seem to be evenly distributed through the whole organ, I have practised in over four hundred cases the ligation, at intervals of a week or more, of first the two inferior thyroid vessels and then the two superiors. The inferior arteries can be reached most easily by a three-inch vertical incision along the posterior border of the lower end of the sternomastoid muscle. The guide is the outer edge of the scalenus anticus. After dividing the fascia over the latter, the incision is deepened by blunt dissection in front of the phrenic and behind the internal jugular and common carotid. The inferior thyroid can then be readily felt or seen as it passes upward and inward along the inner border of the scalenus anticus. Its double ligation, without section, seems practically all that is necessary. The postoperative pain is very slight, but after the ligation of the two superior vessels the pain and dysphagia are always quite severe, and are no inconsiderable factors in the following and inevitable "exacerbation" of the disease. A week or ten days later there need be no hesitation in tying through the usual collar incision the two superior vessels. This operation of quadruple ligation is by no means ideal, but experience shows that it involves no danger of a subsequent atrophy of the gland and the consequent irremediable myxedema. Especially in the presence of marked exophthalmos, it involves much less postoperative danger and much less risk of a therapeutic failure than the usual extensive excisions. The recovery to the normal, or to the hypothyroid asthenia of convalescence, which seems to be the primary disturbance, is usually quite gradual and may be complicated by the development of one or more toxic adenomata which were possibly unrecognizable in the original diffuse hyperplasia. Under these conditions there will be need of a third operation to enucleate or excise the more localized disease. But

this is not an uncommon occurrence after the radical operations, especially when they are preceded by the preliminary ligations. In all of these hyperthyroid cases, however, surgery should be regarded as only a part of the treatment.

After any operative interference the persistence of the symptoms of too much visceral, cutaneous and vasomotor drive should be regarded as indicating some failure in the normal check mechanism which is supposed to aid the thyroid epithelium to retain or metabolize the necessary iodin. As adrenal feeding experimentally increases the content of this element in the dog's gland, it is reasonable to administer by mouth 10 to 15 drops of the adrenal "residue" (as at present it seems the most efficient adrenal derivative) every three or four hours. When the gastrointestinal tract is very active, the 1 gr. tablets, containing in each 10 per cent of the adrenal nucleoprotein material, are sometimes more helpful. It is also reasonable to add a very small amount of iodin, preferably in the form of 3 or 4 drops of the official tincture, in a half-glass of water once daily. But if it should be followed by any swelling of the thyroid or by a feeling of pressure or constriction the dose of iodin should be postponed or stopped. If iodin is continued under these conditions there is danger of aggravating the symptoms.

As convalescence approaches, and in the more ideal operations or those in which all or most of the hyperplasia has been excised, it may appear within a few days, the hyper symptoms change to hypo, or too little drive. There is pallor, lack of appetite and lack of intestinal activity, and the heart and respiration become quiet. The indications in this stage then are those of the probable original disturbance, or hypothyroidism. There is indicated thyroid feeding, and the least "toxic" or the most commonly helpful is the thyroid nucleoprotein material. One-grain tablets containing 2 per cent or 5 per cent of this substance can generally be given every three or four hours and continued indefinitely. Occasionally, especially if there is marked inactivity in the gastrointestinal tract, the thyroid residue in 5 to 10 minim doses at the same intervals may prove more beneficial. Experimentally, this preparation is a most vigorous stimulant for the gastric and pancreatic secretions. At the same time, and for a long period, the patient should be relieved from all conditions which require expenditure of energy. But his or her thyroid gland, even under the most favorable circumstances, should always be regarded as "weak" or prone to fail in its "drive," and so give rise first to the hypothyroid neuroses, which should be met by feeding, preferably, some nontoxic thyroid derivative to prevent the process from advancing or relapsing into the more serious hyper disturbance.

The acute or subacute postoperative toxemia, which is generally regarded as an exacerbation of the preëxisting hyperthyroidism,

is accompanied by a dry skin and by nausea and vomiting and constipation or signs of gastroenteric failure. If it lasts long enough there is enlargement of the liver and spleen and jaundice. The rising pulse and temperature are accompaniments of any toxemia. The thyroid in these conditions shows almost a complete absence of colloid from the alveoli, which, instead, are filled with a mass of cells and granular material. The condition seems, therefore, to be one which is not the result of too much thyroid product and, clinically, the failure of the gastrointestinal tract and probably the liver supports this assumption. For these reasons I have not hesitated, whenever the postoperative course becomes threatening, to administer hypodermically 20 to 30 minims of the liquid thyroid residue every four to six hours.* This treatment does not increase the pulse-rate but rather lowers it, and also the temperature, and relieves the evident failure in the abdominal viscera and thus seems to have saved several of these very dangerous cases.

Summary. 1. The hypo- and hyperthyroid conditions are interchangeable and are manifested by neuroses chiefly of the autonomic group of nerves.

2. The hyperthyroid neuroses do not represent a primary and vicious overactivity of the gland, but seem to develop secondarily from some preceding deficiency in the biochemistry either of the involuntary nervous system or of the thyroid.

3. The hyperthyroid symptoms are traceable to certain "hyperplastic" alveoli in the gland. When all, or the greater part, of these alveoli can be excised the symptoms quickly subside to those of the initial and underlying hypothyroidism.

4. If the hyperplastic alveoli are scattered diffusely and evenly throughout the entire "goiter" the safest and best surgical treatment is to ligate first the two inferior thyroid arteries and later the superior vessels.

5. The convalescence after any surgical intervention may require weeks or months of treatment with adrenal feeding and iodin to support the "check" upon the thyroid, or with thyroid feeding in the form of some "nontoxic" thyroid derivative to correct the primary hypothyroidism and to prevent its relapse into the secondary hyper disturbance.

* The thyroid and adrenal preparations mentioned above were originally made and tested in the Department of Experimental Therapeutics, Cornell Univ. Med. College. They can now be obtained from Schieffelin & Co.

THE INFLUENCE OF OLIGURIA ON NITROGEN RETENTION IN THE BLOOD.*

By O. H. Perry Pepper, M.D.,
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The influence which a marked reduction in the quantity of urine may have on the excretion of nitrogen, and so indirectly on the level of nitrogen in the blood, does not seem to receive adequate recognition. The principle is well known, but it has not been sufficiently applied, and certain points which it seems to make clear have therefore been left in confusion and uncertainty. It is in the problems of nephritis that these principles find their most important application.

In acute nephritis, for example, there is often a decrease in urinary output, a failure to excrete sodium chlorid and a moderate rise in the level of the various fractions of the noncoagulable protein of the blood. In such cases it is frequently assumed that there is impairment of the urea-excreting function of the kidney, as well as interference with the elimination of water and salt. Some even dignify these cases with the name "mixed nephritis." When the evidence is examined, however, one cannot help being impressed by the fact that the nitrogen retention may in some instances be the result solely, or in large part, of the interference with water elimination and that the urea-excreting function of the kidney may be entirely unimpaired. If this view is accepted, a number of apparently contradictory observations become harmonized. Let me review certain of the facts touching on this matter and let me employ urea as representative of the group forming the noncoagulable protein of the blood.

It is the function of the kidneys to maintain the normal composition of the blood and under normal conditions normal kidneys accomplish this result. Under abnormal conditions, however, even normal kidneys may not be able to perform this task and may fail to keep pace with the demands made upon them. For example, an unusual formation of urea may temporarily exceed the kidneys' excreting capacity, and an increase in the blood urea nitrogen will occur. Such an unusual increase in urea content may result from a variety of causes, such as excessive protein diet, rapid destruction of body protein as perhaps in certain acute infections and intoxications, experimental introduction of urea, etc. It is obviously a fallacy to assume, on the basis of such an increased blood urea nitrogen that there is any insufficiency of renal functional capacity. Other evidence is required. Furthermore, the

* Read before the Section on Medicine of the College of Physicians of Philadelphia, March 27, 1922.

blood urea nitrogen may increase simply from rapid concentration of the blood, as when water is lost to the body so rapidly that the concentration of urea nitrogen in the blood rises despite the activities of normal kidneys. This may occur, for example, from diarrhea, sweating or even from diuresis of urine of low concentration.

Even the normal kidney has a limit to the amount of solids which it can excrete in a given amount of urine, and for urea in the human this maximal concentration is put down by Ambard[1] at 5.6 per cent. This high figure, however, was only obtained after feeding large amounts of milk casein and permitting but little water intake. MacLeod,[2] alone, apparently puts it at a higher figure, but it is possible his statement is made in reference to the urine of dogs. Cushny[3] says, "These limits of concentration appear to be fixed by the energy which the kidney can bring to act against the osmotic resistance." He gives the upper limit of urea concentration in human urine at from 4 to 5 per cent. Up to this limit, which, however, is seldom reached, the rate of urea excretion per unit of body weight has been shown by Austin, Stillman and Van Slyke[4] to increase in the normal approximately in a simple direct proportion to the blood urea concentration, and secondly, in proportion to the square root of the rate of volume output of urine per unit of body weight as long as the volume rate remains within ordinary limits. There is apparently a limit above which a rise in the urine volume to any height fails to further accelerate urea excretion. Also, there may be a limit above which a rise in the blood urea concentration will fail to increase excretion. So it is clear that the rate of excretion of urea is limited by the kidneys' concentration ability, which is often reduced in disease of the kidney, and by the amount of urine excreted, which is markedly reduced in still other types of renal disease.

Ambard logically points out that if the concentration maximum is known, the least amount of urine required to permit the excretion of any stated amount of urea is also known. This he terms the "volume obligatoire." Thus, for example, if the level of urea production remains at about its usual level of 30 gm. per day the least amount of urine in which normal kidneys could excrete this would be about 500 cc.

When we turn to the consideration of nitrogenous retention in the blood in kidney diseases we find at once that the various factors which may play a part in bringing about an increase of blood urea nitrogen are not clearly differentiated in most writings of today,

[1] Physiologie Normale et Pathologique des Reins, 2d edition, Masson & Cie, Paris, 1920.

[2] Physiology and Biochemistry in Modern Medicine, 3d edition, St. Louis, Mosby, 1920.

[3] Secretion of Urine, London, Longmans, 1917.

[4] Jour. Biol. Chem., 1921, **46**, 91.

nor is sufficient weight placed on the reduction in the quantity of urinary output.

In acute or chronic nephritis with edema there is quite constantly a diminution of the amount of urine—perhaps due to factors leading to a retention of water in the tissues or to a failure of the kidney to secrete the water. Such urine as is passed is high colored, concentrated and shows a high specific gravity and usually a high concentration of urea and other substances. If there is complete anuria then all of the water, urea and other substances which do not leave the body by other routes must remain in the body. If the oliguria is sufficiently marked as to make it impossible for the kidney to concentrate into it all the urea presented to the organ for excretion, then the excess urea must either be retained or otherwise disposed of. Thus an increase of blood urea nitrogen will occur with perhaps no impairment of the kidneys' ability to concentrate, and resulting simply from a diminished output of water which may have its fundamental cause in tissue retention.

This aspect of the production of nitrogen retention was emphasized by French writers—Legueu, Chabanier, Widal, Weill, Ambard and others—in the literature just before the war. They recognized two types of nitrogen retention: The first with a less than maximal concentration of urea in the urine; the second not dependent on interference with the excretion of urea, but partially, at least, due to the output of an insufficient amount of urine. There has been little application of these principles to actual conditions.

Thus, for example, the kidneys normally excrete urea at a concentration of about 2 per cent, and various workers in this field, including MacLean and de Wesselow[5] and Weiss,[6] consider a concentration of 2 per cent as indicative of a fairly efficient urea excreting function of the kidney. At a concentration of 2 per cent the average daily output of urea is excreted in about 1500 cc of urine in the twenty-four hours. Now if for any reason the urinary quantity is reduced to less than a third while the urea production remains at its former level, then the kidney, no matter how normal, must fail to excrete the whole amount of urea even if a concentration approaching the maximum of 5.6 per cent is reached. It is apparent, therefore, that the oliguria of acute nephritis must of itself sometimes lead to a failure of urea excretion, due simply to the urinary quantity being inadequate to carry off the amount of urea produced. This would be true even if the urea production were no greater than usual; but there is reason to believe that it may be considerably increased in many instances coincident with the onset of the acute nephritis.

With a failure of excretion some retention occurs, and that this is usually not more evident may, in part, be due to its gradual

[5] British Jour. Exper. Path., 1920, **1**, 1.
[6] Jour. Am. Med. Assn., 1921, **76**, 298.

development and to the dilution of the blood by retained fluid, and there may occur even at low levels some compensatory elimination of urea by bowel.

Undoubtedly in many cases even of acute nephritis there is some direct interference with nitrogen excretion, but in many instances the degree of retention which occurs can be explained simply on the disturbed water secretion. Some of the so-called mixed cases, supposedly exhibiting evidences of interference with both water and nitrogen elimination, can be explained on this evidence and properly classed among those showing simply interference with water elimination.

In experimental nephritis in animals the occurrence of an increase in the blood nitrogen in instances with supposedly purely tubular lesions has led to some confusion, for the nitrogen retention should perhaps be explained, at least in part, on the oliguria alone and in part by the increased protein breakdown due to the toxic agent employed. For example, MacNider[7] employs uranium nitrate and considers that it produces in the dog's kidney an acute tubular lesion without degeneration in the vascular tissue. When such an acute tubular injury is produced in a dog whose kidney already shows a naturally developed glomerulonephropathy with histologically well-preserved tubular epithelium, the acute injury is expressed by a rapid reduction in the elimination of phenolsulphonephthalein and by a retention of blood urea and creatinin. These animals become acutely anuric and die, and the kidneys show an early edema and necrosis of the tubular epithelium without the development of any acute injury to the glomeruli. From these experiments MacNider concludes that the inference appears allowable, that all of these substances, phenolsulphonephthalein, urea and creatinin, are eliminated by the renal epithelium, and he concludes that this and other evidence tends to minimize the importance of the glomerulus as a functional unit and to emphasize the relative importance of the tubular epithelium.

However, in the four protocols given by MacNider to illustrate the experiments in which naturally nephropathic animals were given an acute kidney injury from uranium or mercuric chlorid an abrupt cut-down in urine output dates from the administration of the nephrotoxic agent, and in the absence of figures giving the urea concentration in the urine it is difficult to say whether these protocols indicate any true impairment of the urea-excreting function of the kidney or whether they simply show the results of the diminished output of urine. It must, however, be remembered that the dog is said to be able to concentrate the urea in the urine to over 10 per cent. Further investigations along these lines are greatly needed.

[7] Arch. Int. Med., 1920, **26**, 1.

On the other hand, that the concentration ability of the kidney for urea may be well preserved in acute nephritis is well evidenced by the figures given in a recent article by Rabinowitch[8] concerning the urea concentration test. He gives his results in 50 cases, of which 6 are put down as having had acute nephritis. Of these 6 cases, 1 concentrated urea in the urine to 4.04 per cent, 1 to 3 per cent and 2 to 2.79 per cent, while of the remaining 44 cases of chronic nephritis only 3 showed a concentration of 3 per cent or over. The total amount of urine for the twenty-four hours is not given, so it is impossible to judge whether any increase in blood urea nitrogen might be attributed to the oliguria.

This aspect of the matter also touches upon the question of the interpretation of functional tests. For instance, there are certain cases in which, with some nitrogen retention, the phthalein elimination remains high. This may in part be explained by the greater concentration ability of the kidney for the dye, so that while a kidney may be able to excrete a normal percentage of phthalein in a very small amount of urine, the rate and volume of urine in the twenty-four hours will be too low for the kidney to secrete all the day's urea. Furthermore, in the so-called urea concentration test the amount of urine passed must be sufficient for the excretion of the urea administered before any conclusions concerning the functional efficiency of the kidneys can be drawn from any rise in the blood urea nitrogen. And it is to be remembered that fluids are stopped for six to twelve hours before the test. The same applies to the use of any "formula" or index based upon the excretion of urea. For example, Weiss points out that in certain cases of mixed chronic nephritis (nitrogen and salt and water retention) the test, in spite of distinct clinical and functional evidences of nephritis, at times fails to demonstrate the degree of renal inefficiency which he assumes is present. He does not, however, discuss the possibility that there may, in fact, be little or no interference with urea excretion and that the retention of nitrogen is due to a simple oliguria, although in one case of chronic parenchymatous nephritis with 29 mg. of blood urea nitrogen, there was a urea concentration of 4.2 per cent in the urine. The total daily output of urine is not given, so that no conclusions can be drawn. Nor in the earlier work on the urea concentration test by Addis and Watanabe[9] and MacLean and de Wesselow[10] are figures given which apply to the question in hand.

Prognostically there is, it would seem, a considerable difference in the significance of the two types of nitrogen retention. As a rule a true impairment of the concentration power of the kidney is a serious and permanent thing, while, as is well known, those cases of nephritis with no other manifestation than edema often recover with little or no residual renal damage. If it is true that there are

[8] Arch. Int. Med., 1921, **28**, 827.
[9] Jour. Biol. Chem., 1916, **28**, 251.
[10] Loc. cit.

cases of acute or subacute nephritis in which the nitrogen retention is only a secondary manifestation of the water retention, then these cases should have a better prognosis than those with the other type of nitrogen retention.

In the treatment of nephritis an appreciation of these principles is important, for they supply a basis for understanding what can be expected of the kidneys in a given condition. They emphasize the importance of maintaining polyuria when the concentration ability is diminished and of decreasing, if possible, the urea production to an amount which the concentration maximum and the amount of urine, indicate that the patient can dispose of. We can do little or nothing therapeutically toward raising the concentration ability of the kidneys, but we can, by avoiding passive congestion and body dehydration, make sure that the kidneys shall have every opportunity to excrete water; and by reducing the protein of the diet and by avoiding tissue destruction as far as possible, we can lower the demands placed upon the nitrogen-excreting function of the kidney and so avoid one factor which undoubtedly favors nitrogen retention in the body.

PERSISTENT LEUKOCYTOSIS IN THE EARLY STAGES OF THROMBOANGIITIS OBLITERANS.

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The thorough clinical and pathologic studies of thromboangiitis obliterans made by Leo Buerger during the past fifteen years leave no doubt of the fact that such a separate and distinct disease entity exists. Occurring, as he has pointed out, in young male Jews, it affects usually the lower extremities, but not uncommonly also the upper, starts as an inflammation of the walls of the smaller arteries and veins and subjacent tissues and more or less slowly leads to thrombosis of the larger arteries. It gives rise to a clinical syndrome that is, as a rule, definitely characteristic.

Commenting upon the symptomatology of the disease, Buerger says: "Severe nonlocalizable shooting pains in the calf or foot, attended with difficulty in walking, or possibly with tender calf muscles with or without vasomotor symptoms, and coldness in the foot with or without obliteration of the dorsalis pedis and posterior tibial pulses, may be the only symptoms. It is only when we compare the history with its further clinical course and pathology, that we can relegate certain indefinite signs to the onset of the affection. In most instances, however, the patient will not seek advice for such initial symptoms, either because they are not sufficiently severe to require the attention of a physician

or because they are incorrectly regarded as rheumatic in origin, possibly due to trauma, to cold, the presence of flat or weak feet, or because they are explained on the basis of some other minor ailment."

Recently a patient, a Jewish physician, consulted Dr. Llewellys F. Barker, stating that he had suffered from intermittent pains in the legs on exertion, which he could convince himself were symptoms of the "physician's usual neurasthenia," were it not for the simultaneous presence of a persistent leukocytosis. He requested that a general diagnostic survey be made in the hope that somewhere in the body something might be found that would explain the pains in the lower extremities and the continued leukocytosis. The case has so many points of interest that at the suggestion of Dr. Barker I have compared it with other similar cases in the records of the Johns Hopkins Hospital, and have decided that, owing especially to the persistent leukocytosis, it should be placed on record in the literature.

CASE HISTORY. Married man, aged forty-four years, white, a Jewish physician.

Complaint. Aching and pain in the hips and thighs increasing to disability on walking; continuous numbness of the left foot.

Family History. Father died, aged sixty-three years, of angina pectoris; mother died, aged sixty-three years, from apoplexy during diabetes; one brother died at forty-five years from Bright's disease; three brothers and five sisters living and well. Wife has congenital heart disease; two children living and well; no miscarriages. No history of tuberculosis, of mental disease or of cancer in the family.

Past History. He has always been well, except for a fracture of two ribs (followed by a pleuritis) in 1909, until the present illness. Habits: tea used in moderation; no alcohol; fifteen to twenty cigarettes a day for many years.

Present Illness. The patient regarded himself as healthy until August, 1918, when after eating heartily at a barbecue, where he had also one drink of "white lightning," he awoke at 3 A.M. with an excruciating pain and a sense of constriction in his lower chest. His brother-in-law said that in this attack his face was black, and a physician who saw him reported that "from the neck up he looked like a man with apoplexy." He was given morphin twice, three-quarters of a grain in all. The physician diagnosed his condition as "angina pectoris." After remaining in bed for ten days, during which he had slight fever (100° to 101°) and tachycardia (pulse 110 to 120), the pain gradually subsided. A little later he consulted Dr. Evan Evans, who had an electrocardiographic tracing made which showed auricular fibrillation. Dr. Evans also stated that there were evidences of sequelæ of influenza in the left

lung, confirmed by roentgen ray. A dull ache in the lower chest persisted, as did neuralgic pains in the left shoulder and arm.

In April, 1921, owing to a sudden illness of his wife, our patient made a hurried railroad trip to visit her, and after a day or two began to have severe pains in his hips and legs after exertion. In four or five days these pains became so severe that he could not get about except in a taxicab.

On returning to his home and resting his condition improved somewhat, but in less than a week the symptoms underwent exacerbation. He could not walk to the office, one block away, without stopping two or three times to rest. As he walked the "ache" grew more and more intense, rising finally to "real pain." He could not move the thighs, but was forced to "swing his trunk"; soon he felt that he must stop and sit down or he would fall down. As a matter of fact he admits that he has never fallen.

At about this time a blood examination was made and the white cell count found to be 22,000 per cmm. Some abscessed teeth were discovered and removed; later on the tonsils were found to be badly infected, and they were removed on July 9, 1921. After this the pains in his shoulder and arm entirely disappeared, but the condition in the legs grew steadily worse.

Another white cell count was made in August, 1921, and showed 18,000 leukocytes. Wassermann tests made by two different men were negative.

Three days before reaching Baltimore the patient, after riding three hours in an automobile, on trying to walk was forced to sit down with his legs straightened out before him no less than three times in the course of four blocks. The pain was, he stated, excruciating. In walking two blocks from the hotel to Dr. Barker's office on the day of consultation he was obliged to stop now and then and lean against buildings. When he is quiet he feels perfectly well. He has tried to make himself think that his symptoms are all due to nervousness, but the persistent leukocytosis and the severe pains convince him that there must be something radically wrong with him. Libido has been much lessened during the past year and potentia has been poor, though ejaculatio has been normal.

Physical Examination. On November 2, 1921 (Dr. Norman B. Cole). Patient is a man, aged forty-four years, lying quietly, without dyspnea. He is ten pounds under his calculated ideal weight. Skin normal. Muscular development and tone fair. Moderate canities, beginning calvities. Contour of the face normal. Eyes protrude slightly. There is a moderate Dalrymple sign, a slight von Graefe, a negative Rosenbach. Convergence well maintained. Pupils equal and regular, reacting equally and promptly to light. Slight hippus. Scleræ moderately injected. Nasal ventilation normal. Dental occlusion largely maintained by dentures (superior

and inferior); considerable retraction of the gums; recently treated for pyorrhea. The tongue is protruded in the midline without tremor; it is moist and with a slight yellowish-white coat. The right tonsillar fossa is empty and the left shows a small tag of tonsil. Pharynx negative. External ears and canals negative. No tenderness over paranasal sinuses or mastoids. No struma. No general glandular enlargement.

Chest well formed. Expansion good and symmetric. Lungs negative except for a few moist rales in the lower left back. Left border of cardiac dulness just lateral from the nipple line in the fifth left interspace on direct percussion. Apex beat feebly palpable in the same locality. Heart rate 96, regular; no heart murmurs; second aorta sound slightly louder than second pulmonic. Blood-pressure: 122 systolic and 78 diastolic. No tremor of the outstretched fingers. Palms dry and warm. Radial pulsations equal and synchronous; radial walls not palpable; brachials not visible; temporals not tortuous. Just in front of the medial condyle of the right elbow a small gland is palpable, due to an earlier infection of the hand.

Abdomen normal in contour; no tenderness; no abnormal masses; no muscle spasm. Liver and spleen not palpable. Hirci and crines pubis rather sparse. Crines of the transverse type. Phallus and gonads normal.

No edema of the shins. Knee-jerks equal and active. Ankle-jerks are equal. Babinski, Gordon and Oppenheim tests negative. No bathyanesthesia. Cremasteric and abdominal reflexes normal. Deep reflexes in arms normal. Chvostek sign negative.

Slight external hemorrhoids present. Tone of rectal sphincter normal. Prostate normal.

No pulsation can be felt in the A. dorsalis pedis, the A. tibialis posterior or in the A. femoralis on either side.

Laboratory Findings (Dr. H. M. Thomas, Jr.). The blood, the stomach contents, the feces and the urine were examined.

Blood Examination. Red blood cells, 5,080,000; hemoglobin, 85 per cent, Sahli; white blood cells, 17,300; color index, 0.85.

Differential count in a stained smear of the white corpuscles showed polymorphonuclears, 59.5 per cent; eosinophils, 1.5 per cent; basophils, 0.5 per cent; small mononuclears, 30.5 per cent; large mononuclears, 3 per cent; transitionals, 4 per cent; basophilic myelocytes, 1 per cent.

No poikilocytosis nor anisocytosis of the red cells. Platelets normal. Blood-Wassermann reaction negative.

Analysis of the Stomach Contents. 40 cc recovered; free HCl 28 acidity per cent, combined acid 38 acidity per cent; total acid 66 acidity per cent. Microscopically, no yeast cells. Neither Oppler-Boas bacilli nor sarcinæ present.

Stool Examination. Dark brown, formed; occult blood, negative; microscopically, an occasional striated muscle fiber seen. No ova or parasites seen.

Examination of the Urine. Reaction acid; specific gravity, 1002 to 1025; no albumin; no sugar; no Bence-Jones body. Microscopically, negative for casts and red blood cells. A few calcium oxalate crystals seen, also numerous shreds of mucus. Phenolsulphonephthalein test: output in two hours, 67 per cent.

Roentgen-ray Reports (Dr. F. H. Baetjer):

Paranasal Sinuses. Frontals, ethmoids and antra clear.

Lateral Skull. Sella of normal size and shape and of the open type. Frontal and sphenoidal sinuses clear. Calvarium negative.

Lumbar Spine. Shows a little sharpening, especially of the upper edge of the third lumbar vertebra, and there are slight spurs on the crests of the ilia.

Impression (Dr. Baetjer): Spine and scaroiliacs practically negative.

Roentgenoscopic Report of Chest and Abdomen. Heart of normal size; slightly globular in shape. Pulsations normal. Aorta not dilated. Lungs not remarkable. Diaphragm smooth. Swallowing normal. Maximal degree of visceral ptosis and hyperactive gastrointestinal tract.

Orthopedic Report (Dr. George E. Bennett). Impression: We are at a loss to give an explanation of the patient's symptoms from a bone or joint standpoint. There is some evidence, however, of shortening of the hamstring tendons, but we believe that these changes are secondary to some general systemic disturbance. The back gives one the impression that there may possibly be an anomaly of the fifth lumbar, but this is not definite.

Laryngologic Report (Dr. Harry R. Slack, Jr.). Impression: there is no focus of infection in the nose, throat or ears to account for an arthritis.

Neurologic Report (Dr. H. M. Thomas, Jr). The patient appears to have had an arthritis in his shoulder, which was relieved by having an abscessed tooth and the infected tonsils removed; but since then this curious disability in his legs has become worse. The history sounds like that of an intermittent claudication, but I do not remember having seen a case in which the pain and cramp were in the thighs and not at all in the muscles below the knees. He has a contraction of the hamstring muscles, and their consistency seems to me to be unusually firm. No other neurologic findings were important. The circulation in the legs is certainly disturbed, and I must acknowledge that I could not feel the pulses at the ankles, or, indeed, in the femoral arteries, though perhaps careful search on repeated examination may reveal them.

Psychiatric Report (Dr. John R. Oliver). Normal findings.

Dental Report (Dr. H. H. Streett). Partial upper and lower dentures. Nonsuppurative pyorrhea with absorption of alveolar crests and damage to central tissues. Radiographs negative. Find nothing to indicate a focal factor.

Basal Metabolism Estimation (Dr. J. T. King, Jr.). The CO_2 output is 3.5 per cent below the expected for the patient's age and sex, indicating a normal metabolic rate. Resting pulse varied from 80 to 88, and the patient took the test comfortably.

Electrocardiographic Report (Dr. E. W. Bridgman). Impression: normal cardiac mechanism. Inverted *T*-waves in the first two leads. The inversion of the *T*-wave in leads I and II suggests either that there is a myocardial weakness or that there has already been administered a physiologic dosage of digitalis.

Polygraphic Tracings (Dr. Norman B. Cole). Jugular vein and brachial artery yield normal curves.

Diagnosis. 1. Thromboangeitis obliterans with intermittent claudication.

2. Persistent leukocytosis with relative lymphocyte increase.

3. Slight myocardiopathy with history of auricular fibrillation, but none now. Slight changes in electrocardiogram.

4. Slight thyreopathy with eye signs and slight tachycardia, but normal basal metabolic rate.

5. Slight undernutrition (ten pounds), with visceroptosis, slight gastric hyperacidity and hypermotility of the gastrointestinal tract.

6. Nonsuppurative gingivitis.

7. Chronic tabagism.

Subsequent History. On November 7, 1921, the patient was admitted to Johns Hopkins Hospital for further observation. While there his white blood count was 19,400 on Nov. 8, 1921, and on one occasion the left posterior tibial artery was felt to pulsate.

As the patient was to spend a few days in New York, he was advised to see Dr. Leo Buerger and Dr. Emanuel Libman while there. In a letter to Dr. Barker, Dr. Libman reported as follows: "My opinion is the same as yours, namely, that he is suffering from a thromboangiitic disease of the veins and arteries. I am not sure that the case belongs to exactly the same group as that which Buerger describes. In other words, I am not sure that a microscopic examination of fresh lesions would show the typical miliary foci with giant cells which Buerger considers characteristic of the early lesions of the disease which he investigated. It would be interesting to know whether the chest attack, which he had some time before the pains in the lower extremities began, was due to an embolus in the distribution of the pulmonary artery.

"The leukocytosis is interesting. I have not particularly noted it as occurring in cases of Buerger's disease. I have discussed this

question with Dr. Buerger, and he tells me that he has made no definite studies concerning the leukocyte count in the disease."

A letter from the patient dated January 1, 1922, states that on restriction of his physical activities, cutting off tobacco and performing circulatory gymnastics outlined for him he has been doing very satisfactorily. The leukocytosis persists; a blood count made soon after arriving home at the end of November showed 18,300 white blood cells; another made on December 31, 1921, showed 14,700.

Discussion. The case is, it is believed, one of thromboangiitic disease of the arteries and veins supplying both lower extremities. The patient is a full-blooded Jew, born in the United States; his parents were citizens of Austria-Hungary. He has smoked cigarettes to excess for many years. After a sudden attack, in 1918, of auricular fibrillation (which subsided) he was well until April, 1921, when he first became troubled with severe pains in the lower extremities on walking. It was then found that he had a white blood count of 22,000. The pain in the legs and numbness of the left foot increased during the next seven months and the leukocytosis persisted. The rather widespread distribution of the vascular disorder with a comparatively low grade of cyanosis without rapid blanching on change of position of the leg left us in doubt as to the exact diagnosis. There was evidently obstruction to the arterial flow in the vessels of both lower extremities. Whether this is or is not due to true thromboangiitis obliterans the subsequent course of the disease alone can decide, though we think it probable.

Arterial thrombosis not associated with any acute infection, not associated with any wasting disease and not secondary to syphilis or arteriosclerosis has led for many years to much speculation as to the factors concerned in its etiology. Mendel called attention to the susceptibility to a second attack of thrombosis and termed the condition "thrombophilia." Before him Erb had pointed out the susceptibility of young male Jews to dysbasia angiosclerotica (or intermittent claudication), and mentioned alcohol and tobacco as contributory factors. More recently the careful and complete studies of Leo Buerger have established the fact that there exists an infectious disease of unknown etiology which produces inflammatory lesions of the vessel walls and perivascular tissues, and subsequently leads to thrombosis with gradual involvement of the larger vessels. There are still many writers who dispute the infectious nature of this process, whereas others claim that typhus fever is a constant precursor.

As Buerger has pointed out, the disease is rarely seen by the physician until its later stages, since only in them, as a rule, are the symptoms of a nature severe enough to lead the patient to consult a doctor. In the case here recorded the patient, a doctor himself, was soon impressed by the persistent leukocytosis and

proceeded on an exhaustive but unsuccessful search for a causative focus of infection. It seems now fairly clear that the infectious process in Buerger's disease is located in the vessels supplying the extremities; and it seems altogether likely, from the study of the case here reported, that if an opportunity were afforded for study of the leukocyte count early in cases of thromboangiitis obliterans a persistent leukocytosis would be revealed.

In 2 of the other 5 cases studied at the Johns Hopkins Hospital a positive Wassermann reaction was obtained, and in 1 the disease had already existed several years. The fourth case had been affected long enough to produce gangrene of a toe, although subjective symptoms were noted only five months before admission to the hospital. The absence of a leukocytosis in these atypical or long-standing cases is not, therefore, to be considered as evidence on this point.

Conclusion. A case is reported of thromboangiitis of the vessels supplying the legs, similar in many respects to Buerger's disease, and the existence in the patient of a well-marked and persistent leukocytosis is emphasized. It would seem probable that a leukocytosis may be found to occur frequently in the early stages of thromboangeitis obliterans; if this be verified the fact would lend weight to Buerger's contention that the process is infectious in nature.

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INJURY OF THE SPINAL CORD IN BREECH EXTRACTION AS AN IMPORTANT CAUSE OF FETAL DEATH AND OF PARAPLEGIA IN CHILDHOOD.*

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I. **Introduction.** Injuries of the spinal cord, or of the vertebral column, due to breech extraction, are frequently discovered by pathologists. On the other hand, such injuries are rarely reported by obstetricians, and disability from such accidents is rarely recognized by those who see older children.

The obvious inference is that serious damage to the spinal cord during delivery is inconsistent with prolonged life.

From a theoretic standpoint any such conclusion is most surprising for several reasons. In the laboratory young animals survive cord transection with great regularity and for indefinite periods, and on the whole show less evidence of shock than adults of the same species.

Babies frequently survive the severe operations necessitated by spina bifida and often live for long periods, even if the operation involves destruction of a considerable portion of the cord.

Many soldiers lived for indefinite periods after receiving wounds which, in addition to severing the cord, injured the lung.

It seems as if some peculiarly fatal factor must be involved if the general impression that obstetric cord injury is inconsistent with prolonged life is well founded, yet it is hard to see what it can be.

One of the most obvious explanations is that the injury to the cord is always high enough to involve the medulla or the phrenic nerves. This theory is untenable, because there is considerable reliable pathologic and clinical evidence against it.

* Read in abstract before the December, 1921, Meeting of the New England Pediatric Society.

It is also conceivable that trauma to the cord is always accompanied by such severe injury to the spine and muscles that babies almost inevitably perish from traumatic shock. A very casual study of the spinal column at birth suggests that this is an unlikely explanation, as the infantile vertebræ have no such elaborate interlocking bony processes as those seen in adult spinal columns. Furthermore, there is good reason to believe that babies, during a period of several years, can suffer severe cord injuries without serious shock or gross damage to the spine.

If no adequate reasons exists for believing that all babies with traumatic cord lesions die early, and if such injuries can be shown to be common, it is reasonable to suppose that some of them survive and are not properly classified.

These theoretic considerations are of absolutely no interest unless it can be proved that a fair number of such cases are now living with definite signs which can be logically referred to accidents during breech deliveries.

Before reporting cases it is necessary to review, very briefly, certain papers in order to show the development of the present standards of diagnosis of severe cord injuries and to consider a few studies of obstetric traumata.

II. **Bastian's Law.** Up to 1890, as Riddoch points out, clinicians were observing with interest and understanding the spectacular experiments of physiologists on "spinal" animals. Very generally they accepted the obvious conclusion that reflex activity might be expected below the level of a cord transection in man. In that year Bastian, apparently exasperated by the tendency to draw conclusions from the study of laboratory animals and to apply these conclusions to man, collected a number of cases and overwhelmed the clinicians who were influenced by laboratory results. His observations, more or less misinterpreted and misquoted, led to very general acceptance of the theory that reflex activity was practically negligible below the level of cord transection in man. Even Sherrington apparently accepted this point of view.

This polemic paper of Bastian's, destined to exert a profound influence on neurologic progress for a quarter of a century, begins with the following statement:

"The physiologist, by reason of his observation on certain of the lower animals, seems to have instilled into the minds of clinical observers the notion that when the spinal cord is absolutely cut off from communication with the encephalon the reflexes dependent on the spinal cord below the point of section will, in the course of a very short time—that is, as soon as the immediate effects of shock resulting from the operation have subsided—exhibit themselves in an exaggerated manner."

He follows this belligerent opening with reports of cases of cord transection, most of whom died within a few days or dragged out

prolonged existences made miserable by bed-sores or cancer. There is no reason to doubt the accuracy of Bastian's observations, though the following extracts from his case records show his state of mind and incidentally reinforce the present standards of diagnosis.

Among the records is one from a colleague. The patient "died of exhaustion in connection with bed-sores and bladder troubles." The record shows that although knee-jerks had been absent and anesthesia present for a month, "involuntary contractions of the legs, causing them to be completely flexed, are more marked—they move at the least irritation of the skin." In another case, where a fracture-dislocation at the sixth cervical vertebra caused the lesion, the report by Tooth shows that on the twentieth day sole reflexes were present and a feeble knee-jerk was obtained. Postmortem examination proved the lesion to be a practically complete transection. In regard to this case Bastian observes: "This is not a very conclusive case, I merely quote it for what it is worth, it at least suffices to show that there was no exaggeration of reflexes."

Largely as a result of this paper, supported by another by Bowlby in the same year, clinicians for twenty-seven years have taught that cord lesions in man did not allow reflex activity at all comparable with that observed in animals similarly injured. As generally understood, Bastian's law is as follows:

High thoracic or cervical transections produce paralysis of the legs and abdominal muscles and anesthesia and loss of tendon-jerks. The bladder is at first atonic, but later empties itself partially. That is, transections in man cause, essentially, flaccid paralysis and incontinence of urine.

It is clear enough, on careful reading of Bastian's paper, that nothing in the case reports, or in his own conclusions, justifies the statement that permanent flaccidity always follows cord transections in human beings. In fact, there are numerous contradictions to any such assertion. But the tradition was started and, in spite of sporadic protests, it was generally accepted. As a result the diagnosis of cord transection is not made, as a rule, in the presence of reflex activity of the legs.

III. **Study of Cord Transections Due to War Wounds.** The work of Head and Riddoch forces an absolute abandonment of the so-called Bastian's law. These writers were able to study the results of lesions produced cleanly and suddenly in young men, who were at once picked up and cared for under practically ideal scientific conditions. Riddoch states that "any light that has been thrown on the innate functions of the cord is due not only to the unique cases at our disposal but principally to the attitude of mind induced by the monumental work of Sherrington."

The cases thus observed are all entirely convincing, as the degree

of damage to the cord was observed at operation or postmortem and the clinical notes were made by accurate observers. Therefore the results may be taken as conclusive. In healthy men cord lesions amounting to high physiologic transections cause the following signs:

First Stage. Muscular flaccidity with toneless skeletal muscles, anesthesia, dry, easily damaged skin and retention of urine and feces.

Second Stage. After a few weeks reflexes appear. At first nocuous stimulation of the soles causes various toe movements. Later a variety of flexor responses can be elicited by stimulation of any part of the leg or lower abdomen. With severe stimulation both legs and recti abdominis share in a vigorous mass reflex, which is accompanied by evacuation of the bladder. The easy elicitation of this mass reflex, accompanied by sweating, from stimulation of the legs or abdomen is characteristic of the stage of reflex activity. Tendon-jerks and other signs of extensor excitability are later signs. The bladder becomes "automatic," emptying itself at definite degrees of pressure without other stimulation, or at lower pressures when the mass reflex is evoked. In adults a definite coitus reflex can be obtained on genital stimulation.

Third Stage. If sepsis of serious importance supervenes, the reflex activity subsides or even disappears and sometimes never returns. Obviously sepsis occurring prior to the second stage may prevent the occurrence of reflex activity of any kind.

Naturally, Bastian, working with cases complicated by sepsis or malignant tumors, saw few evidences of reflex activity. Further he apparently started with distrust of the physiologist deep in his being. Head and Riddoch, profoundly impressed by physiologic data, had an opportunity to work with men whose wounds practically duplicated laboratory lesions. Their results confirm the physiologic workers while explaining the results of Bastian.

IV. **Obstetric Cord Lesions.** Bruns quotes C. Ruge as authority for the statement that injury of the vertebral column was found in 8 out of 64 babies dying during or after breech deliveries. I have not been able to find Ruge's original paper. However, Warwick, who has published reports on a series of autopsies on the newborn, states that all cases of vertebral damage in her series were accompanied by cord laceration, so it seems fair to assume that serious cord injuries may have been present in Ruge's cases. In 136 infants in whom the central nervous system was examined Warwick discovered cord injury in 3. If, as seems probable on clinical grounds, this injury occurs almost exclusively with breech extractions, Warwick's figures show a very high proportion of such injuries, as not over 10 of her cases were likely to have been breech deliveries.* Moreover, as her series is made up of cases

* In a personal communication Warwick states that the three cord injuries occurred in babies delivered by version.

of all sorts, worked up by different people, it is entirely possible that the whole cord was not examined in every case. The fact that all her cases had cervical lesions suggests the same possibility.

The most striking article is one by Stoltzenburg published in 1911. This observer found gross lesions of the spinal column in 9 out of 75 babies dying of asphyxia, 8 followed breech extraction. In other words, over 10 per cent of the "asphyxial" deaths in her series followed injury of the spinal column during breech extraction. The cords showed no gross evidence of laceration.

In one large obstetrical clinic in this country similar findings are common, though published reports are not at present available.

Clinically the evidence is definite enough that paralysis due to cord transection at birth has long been known. In a recent article Kooy reviewed the literature and reported that, except for his own case, he found no record of any child surviving severe cord injury more than six months. His own case lived nine years, with almost complete anesthesia, incontinence of urine and feces and spasticity of the legs. The lesion was attributed to violence incident to a very difficult version and extraction. The pathologic examination showed a low thoracic lesion with one ventral pyramidal tract still intact.

Burr recently reported 2 cases, 1 confirmed by autopsy. Both babies were born by breech extraction and both died within five months. One showed reflex activity on pinprick but no tendon reflexes. The autopsy in this case showed that the cord was a mere fibrous band between the fourth cervical and first thoracic segments. The other child showed anesthesia and flaccid paralysis suggesting a complete cervical transection. No reflexes were obtained.

Beevor reports a baby, born by a difficult breech extraction, who showed paralysis of the muscles of one arm, and of the chest, abdomen and legs. Anesthesia corresponded. At autopsy evidence of fracture-dislocation of the third cervical vertebra was found, and below the level of the lesion, practically complete destruction of the cord, presumably as a result of hemorrhage and fibrous tissue formation.

Friedman, in an analysis of 2000 cases seen in the neurologic service at the Children's Hospital, Boston, found only 1 diagnosed as cord injury due to dystocia. His case showed flaccid paralysis and anesthesia. Again a history of breech extraction was obtained.

From this cursory review of the literature several conclusions can be drawn: In the first place cord lesions, as a consequence of breech extractions, are not infrequent. Second, they are usually recognized only when accompanied by flaccid paralysis and anesthesia—that is, when the clinical picture conforms to the so-called Bastian's law. Third, in the reported cases the babies almost

invariably died after a few weeks or, at most, a few months of life. Fourth, in the light of the work of Head and Riddoch it seems entirely likely that such babies will show high degrees of reflex excitability provided the lesion is not high enough to involve the medulla or the phrenic nerves or low enough to destroy the lumbar enlargement. The routine care of a baby provides cleanliness and reasonable freedom from chance infection. Under these favorable circumstances indefinite existence seems quite possible.

CASE REPORTS.

CASE I.—*Obstetric Lesion with Widespread Cord Destruction. No Reflex Activity.* J. B., a male baby, two weeks of age, was seen in the neurological out-patient department in November, 1920.

The mother had had several children without any trouble. This baby was delivered by a thoroughly competent doctor, who referred the case with a note giving the following history: The child presented by the breech. Great difficulty was occasioned by the extension of the right arm. During the manipulation necessary to free this the child became weak and rapid extraction, with considerable force, was necessary. Asphyxia required attention. For the next few days he showed tension at the fontanelle and strabismus, and he had convulsions. These signs cleared up, leaving paralysis as at entrance.

When I first saw him he was in a wretched condition. His skin was dry and he was nursing poorly. His right arm was hanging at his side with inward rotation at the shoulder, extension at the elbow pronation and flexion at the wrist and tight flexion of the fingers. Feeble motions at the wrist and of the fingers were possible. Deviation of the hand to the ulnar side was apparently due to weakness of the supinator longus.

No signs suggested cranial nerve lesions, the pupils were equal and reacted, the fontanelle was level and the left arm appeared normal.

The remainder of the body showed flaccid paralysis of the abdominal muscles and of both legs.

Urine dribbled from the urethra, pressure on the abdomen caused evacuation of the bowels and a free flow of urine. Sensation was as shown in the chart. The black area (on the accompanying chart) was absolutely anesthetic, the shaded area more doubtful, but almost certainly involved.

A tentative diagnosis of hemorrhage into the cord as a result of avulsion of some of the upper roots of the brachial plexus was made. Roentgen-ray study showed no evidence of dislocation or fracture. Lumbar puncture showed cloudy yellow fluid under slight pressure. Unfortunately no manometer was used but the sinking of the fontanelle, as fluid flowed from the needle, apparently

ruled out obstruction at the site of injury. Microscopically abundant changed red cells were found.

The question of surgical intervention was considered. The possibility of relieving pressure by laminectomy did not seem worth taking risks for, as lumbar puncture had demonstrated that there was no obstruction to the flow of fluid past the point of injury.

Since entrance to the department the condition of the baby has not improved appreciably. The bladder and rectum became, at six weeks, "automatic." Absolutely no other evidence of reflex activity has occurred in twelve months. The arm is slowly improving with fairly free motion at the fingers, the wrist and the elbow, but inward rotation and pronation persist as in ordinary obstetric paralysis, due to plexus injury. The skin is still dry but intact.

The abdomen and legs show extreme muscle atrophy. Anesthesia is as at entrance.

Comment. The lesion here is obviously one of the cord. Possibly two lesions exist, one of the plexus and one of the cord. The type of arm palsy, with the equal pupils, rather suggests a peripheral origin for the arm paralysis. To me a more logical explanation is that avulsion of some of the cervical roots caused a hematomyelia, which resulted in an almost complete destruction of the lower thoracic and lumbar cord. Such a lesion would explain the striking and persistent flaccidity of the abdomen and legs. Beevor's case, quoted above, showed a quite comparable pathologic and clinical condition.

Treatment is of course purely negative. It is interesting, however, that no catheter was necessary in this or in subsequent cases.

Prognosis is entirely hopeless, as far as I can see.

CASE II.—*Obstetric Transection with Reflex Activity.* F. Y., a girl of three years, was transferred to the neurological department from the clinic of the Harvard Infantile Paralysis Commission, to which she had been referred by her physician.

She was the fourth child. Five years before her birth her mother had infantile paralysis involving one leg. Delivery at eight months was required as a result of nephritis in the mother. A difficult accouchement forcé was done and considerable difficulty was encountered in the version and extraction of the child. For weeks the baby was very ill and was not expected to live from day to day. Gradually she gained strength and seemed to thrive, but has never sat up or attempted to stand. She has never been conscious of movements of the bowels or emptying of the bladder. She has never had any serious acute illness.

When she entered the neurological out-patient department May 9, 1921, the physical examination was as follows:

She was a cheerful, intelligent child, lying comfortably with

legs abducted and semiflexed at hips, partly flexed at knees and extended at ankles. The upper extremities and head and chest were normal throughout. The abdomen was moderately distended and the muscles of the abdominal wall were flaccid. No voluntary movements were seen below chest. Development of legs was normal. The skin was clear and moist.

Reflexes were as follows: knee-jerks were difficult to get and when obtained were atypical, as the adductors contracted strongly and the quadriceps only slightly. They were the same on the two sides. Ankle-jerks were very much more lively than the knee-jerks. Attempts to obtain clonus led to curious responses. Occasional typical sustained ankle or patellar clonus was elicited in the usual way. Irritation of the skin over any part of either leg or just above the symphysis led to clonus of the whole lower extremity, sometimes spreading across and involving the opposite side. This manifestation was usually followed on further stimulation by abrupt strong flexion reflexes, including urination.

Stroking or gentle pressure on the sole of the foot caused Babinski's phenomenon and occasionally strong extension suggesting the extensor thrust in laboratory animals. Chaddock's, Gordon's and Oppenheim's reflexes were present.

Definite flushing of the skin on stroking was present, ending sharply at the upper border of anesthesia.

Roentgen rays of the spine were negative.

No important changes have taken place since she was first seen.

Comment. This child shows anesthesia and absence of voluntary motion below the chest, corresponding with the signs to be expected from a severe lesion at the seventh dorsal segment. The flaccid paralysis of the recti abdominis suggests that several segments are almost completely destroyed. The legs show lively reflex activities, chief among which are the flexion reflex as described by Head and Riddoch and extensor phenomena suggesting the extensor thrust of the spinal animal. Vasomotor disturbances and the automatic bladder and rectum conform to the picture of transverse lesions as now understood. The prominent extensor phenomena suggest that the lesion may not be absolutely complete.

Obstetrical injury can be assumed in view of the history of the difficult extraction of a premature baby.

Prognosis as to the restoration of functional communication with the brain seems hopeless. Later on, orthopedic apparatus may possibly be fitted which may make some locomotion possible.

(This child was again seen in May of 1922. At that time there was slight but definite sensation over legs and abdomen. Orthopedic apparatus was fitted and muscle training begun. After a few weeks definite voluntary movements appeared. The child in October walks with apparatus and support though all motions are very slight. However, enough motion and sensation are evident

to warrant hope of some functional recovery after four years of anesthesia and paralysis. There is also consciousness of sphincters though no real control has been obtained.)

CASE III.—*Obstetric Transection with Reflex Activities.* E. T., a girl, born February 9, 1919, was seen in February 1921, and repeatedly since then.

She is the only child of healthy parents, born with great difficulty, with forceps to the after-coming head. No asphyxia or convulsions followed. For a few months she was very weak, moved very little and was not expected to live. Then she seemed to thrive, except for the fact that she could not sit alone until over a year old, and has never attempted to stand. According to the mother she controls her rectal sphincter but not her bladder.

When I saw her first she was a very cheerful, active child as far as head, chest and arms went. Below the line shown in the chart she was absolutely a reflex mechanism. Anesthesia was complete. On the left she retained control of the upper segments of the rectus abdominis. The rest of the abdominal wall was flaccid and without reflexes. The back showed marked weakness below the ribs and she tended to slip forward unless supported.

The legs were in semiflexion at hip, knee and ankle. Reflexes were as follows: knee-jerks and ankle-jerks present—not active. No clonus. Babinski and associated phenomena present. Painful stimulation caused active, quick flexion of hip, knee, ankle and toes, with inconstant urination. The receptive field for this reflex extended over both legs and for a short distance above the symphysis. By gentle, steady pressure occasional typical extensor thrusts could be elicited.

In general the muscles showing these reflex activities were not spastic—in fact, they gave the impression of flaccidity when not active. While under observation in the wards the child showed no signs that she was conscious of reflex activities or of urination or defecation, and she was not in any way upset by lumbar puncture, which showed no abnormality of fluid or pressure.

Attempts to measure the activities of the bladder, after the method of Head and Riddoch, failed, as the child urinated at once when the catheter was introduced. Genital manipulation caused an extreme flexion response.

Flushing of the skin below the level of anesthesia was marked. The skin was soft and moist.

The development of the legs was normal. Roentgen rays showed no abnormality of the spine.

Comment. This child shows a picture of reflex activity practically identical with that seen in laboratory animals and one that is quite comparable to that described in man. The lesion is probably due to hemorrhagic softening of the cord over several of the

lower thoracic segments, and presumably is the result of manipulations during delivery.

The mother of this child had been assured that the appearance of reflexes meant later control of muscles. Of course, this prognosis is not justified. In fact it is entirely likely that any severe infectious disease will result in loss of activity.

Fitting of orthopedic apparatus may allow a certain amount of activity later.

CASE IV.—*Obstetric Transections with Reflex Activity.* M. P., a boy of thirteen months, was brought to the hospital in May, 1921, because he could not walk or sit up. He has been followed in the out-patient department since entrance.

He was the first child of healthy parents. A friend of the mother, who helped at the delivery, gave the following account of the procedure: The mother was etherized and the doctor started on a breech extraction. Four people held the mother in bed while the operator, with his feet braced against the side of the bed, pulled. Suddenly, he said, "Something broke." Immediately afterward the child was born, apparently dead, but after a few hours, without efforts at resuscitation, he began to cry. For the next week he seemed likely to die at any moment, but gradually began to nurse well. Since then he has done well, except for inability to sit up. No definite bladder or rectal disturbances have been noticed. The legs are said to have shown movement for many months.

Physical examination shows a well-nourished, evenly developed baby, perfectly comfortable, lying with legs extended. The head and arms seem normal and the chest muscles of respiration seem to be acting normally. The abdomen is protuberant. No voluntary motion noticed in the legs.

Sensory examinations shows anesthesia below the nipple line.

No vasomotor changes are obvious. The skin is clear and moist.

The abdominal and lower back muscles are flaccid and without reflexes. The muscles of the legs are relaxed and passive motion shows no evidence of spasticity or contractures. Both legs show definite lowering of muscle tone, and knee-jerks and ankle-jerks cannot be elicited. No ankle-clonus.

Reflex activity occurs as follows: on stroking the foot or lower leg on either side Babinski's phenomenon appears. Nocuous stimulation, as by pinch or pinprick, changes the character of the response abruptly, and the whole flexion reflex, including evacuation of the bladder, is started. On severe stimulation this reflex is shared by the opposite leg. The receptive field of this reflex appears to extend from just above the symphysis to the toes. In addition the crossed extension reflex can be easily elicited at times, that is, flexion of the stimulated leg and extension of the other.

Roentgen rays show no abnormality of the spine.

Comment. As a basis for discussion of the symptoms of transverse lesions this child is most satisfactory. First, there is no question as to the possibility of rupture or other cord lesion resulting from the spectacular method of delivery. Second, the absence of deep reflexes would reconcile Bastian's followers to the diagnosis. Third, the reflex activities show great similarity to those seen in the physiologic laboratory, or in war hospitals where Head and Riddoch did their work.

The lesion is evidently in the lower thoracic region, with its upper border about the fifth segment, extending down, as suggested by the flaccid abdominal wall, to the tenth.

CASE V.—*Obstetric Injury to the Cord with Signs of Incomplete Cervical Transection.* E. H., a girl of twelve, seen in consultation with Dr. R. W. Lovett, and Dr. F. R. Ober, of Boston, on October 24, 1921.

She is the only child of healthy parents.

She was delivered at full term by a well-known and competent obstetrician. The child presented by the breech. A gauze fillet was used to get traction in the groin. The left arm was extended and required some force for its release. As far as I could gather from the very clear account of both parents no unusual force was used and no anesthetic was used or needed. Afterward, in response to questions, the nurse said the delivery was "done too quickly."

After birth the child showed the following signs:

1. Sunken, almost closed left eye without evidence of any local trauma.
2. The left arm was abducted and externally rotated at the shoulder, sharply flexed at the elbow and hyperextended and supinated at the wrist so sharply that the back of the hand lay on the extensor surface of the forearm.
3. Respiration was noticeably shallow and rapid.
4. Both legs were flaccid.
5. Pinprick over the left arm, body and legs produced no reaction, either sensory or motor.

For the next two and a half years the parents noticed no change. Nutritional disturbances were overcome by careful regulation of diet.

At two and a half years she was operated on for contractures of the adductors and gastrocnemii. Prolonged orthopedic treatment was persistently carried out until she was able to walk at four and a half years. Since then several operations have corrected deformities at wrist and ankle.

At six years, for the first time, she was able to control her sphincters enough to wear ordinary clothing. Since then this control has gradually improved until it is adequate, except on rare occasions.

She now goes to school, dresses herself, combs her hair and, in general, leads an active life, though stiffness of gait and an awkward, weak left arm handicap her more or less. Mentally she is obviously unusually bright. She has never had convulsions.

Physical examination shows a well-developed, alert girl, standing erect in plaster jacket.

Her expression is normal, except that there is definite narrowing of the left palpebral fissure and a small left pupil. No disturbance of any cranial nerve is present. She has no speech defect. She has no involuntary movements of arms or legs.

The neck and throat are normal.

The thorax is asymmetric with absence of movement over the upper left chest. The spine shows a sharply circumscribed scoliosis of the lower cervical and upper thoracic spine, with convexity to the left. There is extreme atrophy of the sternal portion of the pectoralis major and of the intercostals on the left, particularly those between the upper six or seven ribs.

The left arm shows some atrophy of the big muscles about the shoulder, which is held higher than the right. All motions are possible at the shoulder-joint. The upper arm shows strong flexor muscles and a rather weak triceps. The lower arm shows weak flexors and stronger extensors. Functional balance results from tendon transplantation done a number of years ago. The hand shows practically complete atrophy of the small muscles, which, however, retain a very little power, enough to give a distinct functional value to the extremity.

The right arm is and always has been, efficient, but the hand is distinctly thin as compared to the strongly muscled upper arm and forearm.

The abdomen and lower back appear normal.

The legs show moderate spasticity with more marked signs on the left. Various tenotomies and persistent after-care have corrected deformities.

Sensory changes are definite. The evidence for diminished power to discriminate between heat and cold over the area shown in the chart is conclusive. Tubes at 120° and 45° F. were used. Pain sense is less definite, and I thought the element of fear entered. Touch and muscle sense are not impaired. Vibration is well recognized.

Visceral examination shows no abnormality beyond the intrathoracic signs due to the asymmetry of the chest.

Comment. The signs at birth were consistent with an oblique lesion with its upper angle at the seventh cervical segment on the left.

The later course of the case shows that permanent changes in the anterior horn cells have occurred on the left from the seventh or eighth cervical to the sixth or seventh thoracic and probably

in some cells of the eighth cervical segment on the right. The spastic legs can be accounted for by partial destruction of the pyramidal tracts, while the sensory changes may be produced by a hematomyelia destroying the central gray matter or by interference with fibers higher up. As a result of the anterior horn destruction and consequent paralysis of thoracic respiration on the left a compensatory expansion of the right chest has caused a scoliosis. The pupillary changes and the enophthalmos are accounted for by involvement of the sympathetic fibers before emergence from the cord.

From the standpoint of diagnosis there is no difficulty about the case, once it is recognized that obstetric accidents can affect the cord; but it is significant that thirteen successive consultants, including neurologists, pediatricians and orthopedists regarded this case as one of cerebral palsy, and several gave the gloomiest forecasts as to mental development. During the past year our experience at the Children's Hospital with the other cases here reported has kept us on the lookout, and the diagnosis was made in the office of Dr. Lovett and Dr. Ober before I saw the child. A moment's consideration shows that the combination of partial flaccidity of the arm, spasticity of the legs and sensory changes with ocular signs could not be accounted for by any combination of cerebral lesions consistent with life and intelligence.

As far as other possibilities are concerned the history rules them out. Only a traumatic lesion could explain the steady improvement and the present condition.

Discussion. 1. *Pathologic Data.* There is every reason to suppose that pathologic statistics underestimate the frequency of cord injuries. As far as I know no considerable series of autopsies has been reported where the entire cord has been examined. It is fair to assume, therefore, that low thoracic injuries are often overlooked. Furthermore, it seems possible that certain serious lesions might be passed over if routine sections of the hardened cord were not examined.

Physiologically there is a certain amount of pertinent evidence. In the first place, young animals recover from "spinal shock" more rapidly than older ones of the same species. This can be demonstrated easily by comparing the time within which a decapitated kitten begins to show reflexes with the longer period required by the adult cat.

Experience with decerebrate animals also has some bearing on the problem. Ordinarily an animal decerebrated by midbrain section shows a very constant rigidity for many hours. Sometimes this rigidity fails or the animal dies suddenly. Often the only reason appears to be a thin film of blood over the medulla. It is possible that clots from an intracranial hemorrhage might cause

a block of physiologic impulses in the cord. Such a situation, as in one baby I have recently seen, might lead to a diagnosis of cord injury where the real trouble was intracranial.

Further evidence on the question of asphyxia will be considered in connection with obstetric data.

2. *Clinical Data.* The fact that so few previous cases have been reported needs explanation.

In the first place it is obvious that the diagnosis of cord transection is almost never made where reflexes are lively. Of course the work of Head and Riddoch, now universally accepted, will lead to recognition of many hitherto unsuspected cases.

But a more important element enters into the situation. There is so much emphasis laid on the difficulties of focal diagnosis in neurologic disease in infancy that examination is entered on in a spirit of perfunctory despair. Naturally, when knee-jerks, plantar reflexes and sensory signs are regarded as hopelessly confused accurate study is regarded as a rather fatuous procedure.

On the other hand if one looks upon an infant as a rather simple physiologic problem many clues are found. It seems to me that failure to recognize neurologic disorders in babies usually depends on failure to look for gross changes in sensation, for abolition of voluntary activity and for strikingly abnormal reflexes rather than on inaccuracy in detailed examination.

Differential diagnosis is relatively simple if the possibility of cord lesion is borne in mind. In the newborn infant brachial palsy, intracranial hemorrhage and spina bifida are the important alternatives. Pure peripheral brachial palsy is usually obvious enough. Intracranial hemorrhage, if severe or if accompanied by clots in the vertebral canal, may be indistinguishable. Obviously if there is serious intracranial pressure the cerebral condition is the one to watch. Spina bifida, if not obvious, demands roentgen-ray study.

It is a striking fact that roentgen-rays are regularly negative in my series. A possible explanation of this unexpected finding will be given later.

The various atrophies, infantile paralysis, spinal injuries in infancy and so on require a good history rather than any very refined physical examination.

Examination of the spinal fluid in young infants may reveal evidence of hemorrhage, but of course does not localize the lesion. Possibly combined cistern and lumbar puncture, as used by Ayer, might give valuable information where pressure on the cord is suspected.

Treatment is restricted, primarily, to avoidance of contractures and prevention of infection. One thing seems fairly clear: The bladder, if left alone, will take care of itself without dangerous overdistention or urinary sepsis. The fact that trophic changes

are not evident in most of the cases renders timely assistance by optimistic orthopedic men more or less promising.

Prognosis is of course discouraging, but there is no evidence to prove that improvement may not be hoped for. Naturally mental development is not in any way threatened.

3. *Obstetric Considerations.* The obstetrician does not fear cord injury in breech extractions. In the text-books there is no suggestion that well-conducted obstetric maneuvers can damage the cord. Asphyxia is the single recognized danger. To prevent this asphyxia speed in extraction is regarded as essential.

In discussing the subject of asphyxia two grades are distinguished: the livid and the pallid. The first is regarded as unimportant, the second as extremely dangerous. I get the impression that pale asphyxia is thought of as the final stage of blue asphyxia. It is hard to see any reason for believing that there is any such thing as "pale asphyxia." Physiologically, asphyxia stays asphyxia until the blood recovers a sufficient amount of circulating oxygen. Clinically, pure asphyxia, as in choking or in conditions like chlorine gas poisoning, produces cyanosis which persists until adequate relief is given or death ensues.

On the other hand, collapse and death, with pallor and failure of respiration, occur in patients after traumatic shock and in cases suffering from intracranial pressure.

If breech babies do not die of oxygen deprivation what kills them? As far as I know the literature is silent. It is legitimate, therefore, to speculate.

In considering possible causes it is of course necessary to pay special attention to factors which occur only in breech delivery.

Traction on the neck, sharp bending of the spinal column and traction on the brachial plexus all occur in head deliveries.

The two possible forces which appear to operate only in breech cases are:

1. Traction exerted over the entire length of the vertebral column.

2. Direct pressure on the head, resulting from uterine contraction or due to direct suprapubic pressure by the operator or assistant.

The first factor would offer a logical explanation of cord rupture. The spinal column of the infant is obviously extensible. In head presentations the extension takes place only between the head and the shoulders, and presumably the cord can adapt itself to this degree of stretching. In breech deliveries, however, the total increase in length is greater as the column may give at every space throughout the length of the spine.

The spinal cord of the baby is firmly anchored below by the cauda equina. Above in the cervical region short, heavy, almost horizontal roots fix it firmly in place. Its upper end, of course, is continuous with the medulla.

If the spinal column becomes too long one of two possible acci-

dents may occur. The cord may give, with resultant hemorrhage or even rupture, or the cord may hold and herniation of the medulla into the foramen magnum may result. These serious results may theoretically occur without gross bony injury discoverable by roentgen ray.

In the first case more or less definite blocking of physiologic impulses will occur, as in the clinical cases here reported. It is also possible that combinations of various forces may favor avulsion of the brachial plexus roots from the stretched cord.

On the other hand if the cord does not yield the medulla must be pulled down. Just at this moment pressure on the head increases, often to an extreme degree. Theoretically such a combination of forces might cause fatal medullary pressure with vasomotor collapse or extreme vagus stimulation. The logical result would be collapse of just the type which obstetricians call asphyxia pallida.

If these entirely theoretic considerations are reasonable it is clear that the procedure in breech extractions may be based on wrong foundations.

There is some clinical experience that is relevant. Potter, who believes that version is a reasonable method of delivery in practically all cases, pays no attention to ordinary degrees of blue asphyxia. He even cuts the cord before beginning extraction if it is in his way. On the other hand by thorough dilatation, maintenance of flexion, lack of hurry, gentle traction and moderate suprapubic pressure he avoids the combination of severe traction and extreme pressure so often seen in extractions. A further fact, which may be of vital importance, is that he does version as a matter of choice, and, therefore he does not have the uterus contracted down on the head as it is when an ordinary breech delivery is under way. In spite of his apparent lack of fear of asphyxia, his fetal death-rate is not tremendous. It is certainly against all theories in the text-books that a man who deliberately disregards the single cause of death should not kill a very high percentage of his babies.

I have discussed the obstetric bearings at some length elsewhere. It seems quite certain that the traction and suprapubic pressure sometimes exerted in breech deliveries are extremely likely to favor herniation of the medulla.

Without any valid evidence from the obstetrical point of view I believe that there is good reason for investigating the pressure changes within the cranio-vertebral cavity. From a theoretic point of view it seems probable that these change are of as great importance as the chemical changes in the blood,

Conclusions. Five cases are reported in which crippling depends on injuries to the spinal cord apparently caused by breech extraction. In making the diagnosis pathologic, clinical and physiologic facts are considered.

Four of these cases showed conclusive evidence of practically

complete transection. In transections the following syndromes may be expected:

1. High cervical transections are probably all fatal on account of the proximity of the lesion to the phrenic nerves and the medulla.

2. Transections below the fatal level, if accompanied by enough hemorrhage to destroy the cells of the lower segments, result in anesthesia and permanent flaccidity below the lesion.

3. Transections confined to a few segments and not involving the lumbar enlargement will show in succession the following syndromes:

(*a*) Anesthesia with flaccid paralysis. After a few days or weeks the flaccid paralysis will be modified. The infant will then show:

(*b*) Anesthesia, as before, a zone of flaccidity corresponding with the destroyed anterior horn cells, and below this zone, reflex activity of distinctive type. During this stage the bladder and rectum become "automatic."

(*c*) On theoretic grounds it seems likely that this stage of reflex activity will last only so long as severe infection is avoided.

One child showed evidence of an incomplete lesion. She showed flaccid paralysis dependent on destroyed cells and, lower, spasticity from tract involvement, with sensory disturbances and sphincter disorders proportionate to the involvement of cells and tracts.

It is evident that the vast majority of obstetric spinal-cord injuries are caused by maneuvers incident to breech extractions.

From a theoretic consideration of the forces at work in extractions it seems justifiable to suggest that traction on the cord, when combined with suprapubic pressure or uterine contractions on the head, may cause collapse or death from herniation of the medulla through the foramen magna.

If this possibility can be proved by suitable laboratory or clinical studies, it will be proper to challenge the statement, now almost universally accepted, that asphyxia is the only important cause of fetal death in breech extractions.

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VISCERAL ADHESIONS AND BANDS: NORMAL INCIDENCE.

SECOND PAPER.*

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At the last annual meeting of the Gastro-enterological Association, the writer presented the first of a series of papers on visceral adhesions, based upon a study of 297 unselected postmortem sections of all ages and both sexes. This paper was entitled "Visceral Adhesions and Bands. A Preliminary Report."[1] Its object was to indicate the scope, methods, and some of the conclusions arrived at as a result of the investigation being reported upon.

The object of the present communication is to make available in tabular form what may be called a standard of expectation of frequency of visceral involvement by adhesions in both sexes. This standard is given for all ages, and for four separate age periods. The tables themselves are comparable to and based upon the same original material as a table indicating the frequency of visceroptosis in unselected material at all ages, which was presented at the last annual meeting of the American Medical Association under the title "Visceroptosis: Normal Incidence. A Preliminary Report."[2]

There exists in the literature no series of cases with which the present can be compared. Therefore, although it is realized that greater accuracy might have been obtained from the study of a larger number of cases, the present results are offered in the belief that they will prove reasonably reliable, and in the hope that they may at least stimulate other workers to prove their accuracy or otherwise by reporting larger series of cases.

With regard to the tables themselves, it may be explained that the two main age groups "Below Forty" and "Above Forty" include the two other age subdivisions of "Fetal" and "Senile." Thus the age of forty becomes a proven dividing line between youth and age. The column entitled "No. of Obs." appearing in Table I, might better have been entitled "Actual Frequency," since the figures in this column represent in each case the number of positive findings with reference to the total number of cases in each sex group. In Table VI, the column "No. of Obs." indicates the total number of viscera involved by adhesions in the given age-sex group. In

* Read at the Annual Meeting of the Gastro-enterological Association, Washington, May 2, 1922.

Original data for this article obtained in 1912–1914 through the courtesy of Professors Pick and von Hansman, of Berlin, Professor Frankel, of Hamburg, and the students then working in their Institutes of Pathology.

[1] Bryant: Am. Jour. Med. Sci., 1922, **163**, 75.

[2] Bryant: Jour. Am. Med. Assn., 1921, **77**, 1400.

Table VIII, the same column, "No. of Obs." indicates the total number of actual adhesions present in each age-sex group, the number of different types of adhesions that are present in any age-sex group being indicated in the main column of the table. In Table VII, under "Legend" appear for the sake of brevity the expressions "2 to 8 Adhesions Present" and "8 or More Adhesions Present." It might have been more correct and more explicit to have used the phrases "Two to Eight Viscera Involved by Adhesions" and "Eight or More Viscera Involved by Adhesions." With these exceptions, it is hoped that the Tables will prove reasonably self-explanatory.

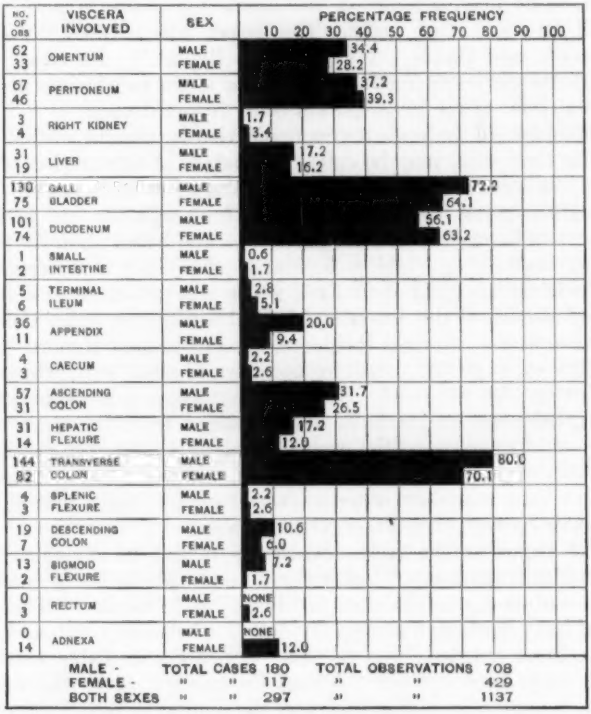
NO. OF OBS
VISCERA INVOLVED
SEX
PERCENTAGE FREQUENCY
10 20 30 40 50 60 70 80 90 100
62 OMENTUM MALE 34.4
33 FEMALE 28.2
67 PERITONEUM MALE 37.2
46 FEMALE 39.3
3 RIGHT KIDNEY MALE 1.7
4 FEMALE 3.4
31 LIVER MALE 17.2
19 FEMALE 16.2
130 GALL BLADDER MALE 72.2
75 FEMALE 64.1
101 DUODENUM MALE 56.1
74 FEMALE 63.2
1 SMALL INTESTINE MALE 0.6
2 FEMALE 1.7
5 TERMINAL ILEUM MALE 2.8
6 FEMALE 5.1
36 APPENDIX MALE 20.0
11 FEMALE 9.4
4 CAECUM MALE 2.2
3 FEMALE 2.6
57 ASCENDING COLON MALE 31.7
31 FEMALE 26.5
31 HEPATIC FLEXURE MALE 17.2
14 FEMALE 12.0
144 TRANSVERSE COLON MALE 80.0
82 FEMALE 70.1
4 SPLENIC FLEXURE MALE 2.2
3 FEMALE 2.6
19 DESCENDING COLON MALE 10.6
7 FEMALE 6.0
13 SIGMOID FLEXURE MALE 7.2
2 FEMALE 1.7
0 RECTUM MALE NONE
3 FEMALE 2.6
0 ADNEXA MALE NONE
14 FEMALE 12.0
MALE - TOTAL CASES 180 TOTAL OBSERVATIONS 708
FEMALE - " " 117 " " 429
BOTH SEXES " " 297 " " 1137

TABLE I.—**Visceral involvement by adhesions. Percentage frequency in relation to sex and age. All ages.**

A glance at Table I indicates that, in the average case coming for examination, the transverse colon may be expected to be involved by adhesions more often than any of the other viscera; 7 women and 8 men out of every 10 presumably have some involvement of this structure by congenital or acquired adhesions. The gall-bladder and duodenum come next in order of frequency of involvement,

these viscera being followed in frequency in the order named by the peritoneum, omentum, ascending colon, and hepatic flexure. The appendix, liver, and descending colon are also involved by adhesions sufficiently often to attract attention on a graphic chart. A study of Table I also indicates that although the difference in the rate of involvement of the two sexes for any given organ seldom varies by as much as 10 per cent, neither sex has an excess of involvement of all the viscera studied. Thus, in the first group of the three viscera

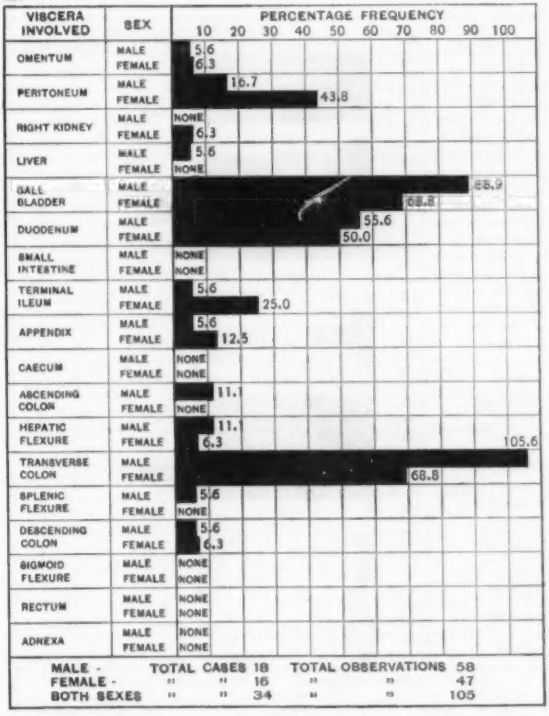

TABLE II.—Visceral involvement by adhesions. Percentage frequency in relation to sex and age. Fetal (12 to 55 cm.)

most often involved by adhesions, the male percentage of involvement is higher than the female with regard to the transverse colon and gall-bladder, but lower than the female with regard to the duodenum. Also, the male percentage of involvement is greater as regards the omentum, ascending colon, appendix, and hepatic flexure, but lower for the peritoneum.

A study of Tables II to V inclusive, allowing a consideration of progressive age changes in both sexes, reveals, as would naturally

be supposed, more facts of interest than can be obtained from the consideration of a single mixed-age table. Furthermore, a study of these tables is sufficient to give a basis for inference concerning the congenital or acquired character of the adhesions found involving any individual viscus.

A careful preliminary study of all the available data, when arranged by successive age decades, caused the age of forty to be taken as a definite point sharply dividing youth and age; this is from

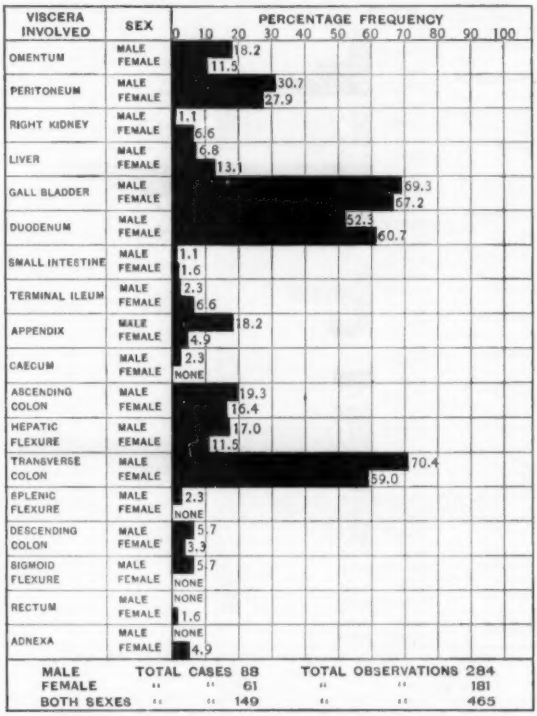

TABLE III.—Visceral involvement by adhesions. Percentage frequency in relation to sex and age. Below forty years of age.

the point of view of adhesive processes within the abdomen. Having arrived at this point in the study, the material at hand was arranged as shown in the tables, in the two main age groups "Below Forty" and "Above Forty," further indication of the relation of age to adhesions being gained by utilizing the two subgroups, "Fetal" and "Senile." Obviously, in the point of total cases, the fetal and senile groups are too small to be more than suggestive; but they are at least suggestive.

The most striking fact about Table II, based upon a study of the fetal group, is that it should be possible to make any table worth showing at all, graphically, since it has for the most part been considered that adhesions in the fetus are the exception rather than the rule. The second striking fact about this table, is that the percentages should run so high for the viscera which are chiefly involved. It is for example rather startling to find 105 per cent of the transverse colons in this fetal group of 18 males involved by

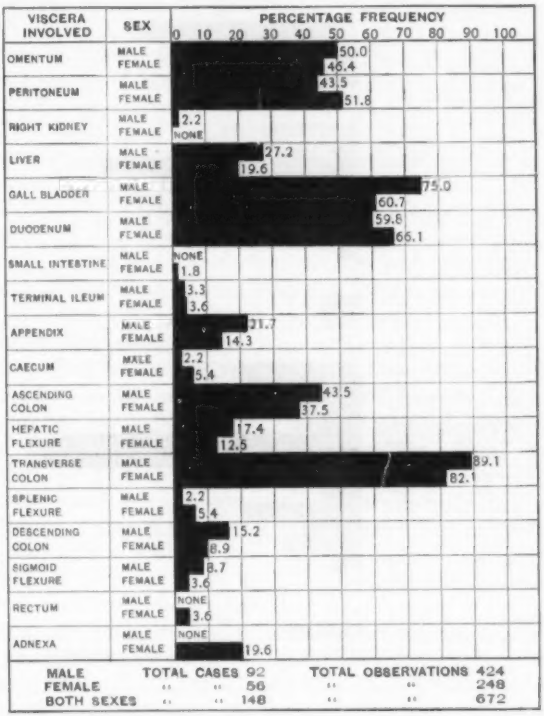

TABLE IV.—Visceral involvement by adhesions. Percentage frequency in relation to sex and age. Above forty years of age.

demonstrable adhesions, this statement being explained by the fact that many of the cases under consideration presented more than one definite band involving the transverse colon. Incidentally, the method of recording the presence of these adhesions may be indicated by the following example: a fetus presents one adhesive band running from the gall-bladder across the duodenum to the transverse colon, and another band running from the ascending to transverse colon; this case would be recorded as having a total of five viscera

involved by adhesions, that is the gall-bladder, duodenum and ascending colon once each, and the transverse colon twice. As in Table I, sex differences in the rate of involvement are conspicuous in Table II. Thus whereas the transverse colon, gall-bladder, and duodenum are involved more often in the male than in the female fetus, the peritoneum, terminal ileum, appendix and omentum are more frequently involved in the female than in the male fetus.

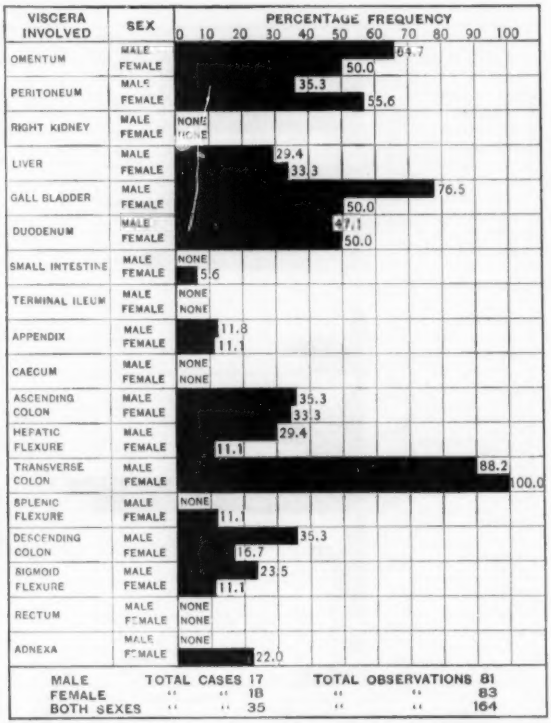

TABLE V.—Visceral involvement by adhesions. Percentage frequency in relation to sex and age. Senile (over seventy years.)

As one studies Tables II to V with reference to the relationship of progressive age to visceral involvement by adhesions, several points of interest are brought to the attention. Among these points of interest may be mentioned the fact that the rate of involvement for any given viscus may either increase or decrease with age in both sexes. Also, the relative frequency of involvement of any special viscus with regard to sex may vary at different periods. One or two examples may be given.

The terminal ileum shows in both sexes a decreasing involvement

by adhesions with progressive age, the rate being distinctly highest in the fetus. Incidently, this finding is diametrically opposed to the dictum of Lane; he has stated that bands about the terminal ileum represent crystallization of lines of force which increase with age, this crystallization resulting from efforts of the organism to support a sagging viscus. The omentum in both sexes is increasingly involved with progressive age; the same progressive increase with age is evident as regards the adnexa of the female, and the sigmoid in both sexes.

The sigmoid flexure is a conspicuous example of a viscus progressively involved with increasing age. No involvement occurs in the fetus in either sex. Below the age of forty in the male there is an involvement of but 5.7 per cent. The rate increases to 8.7 per cent in the male above forty, and the figure for the senile male rises sharply to 23.5 per cent of involvement. The figures for the female with regard to increased age involvement are less striking but the same in character.

The female adnexa present another striking example of what one must look upon as adhesive processes of degeneration. Here, the involvement is but 4.9 per cent below the age of forty, as contrasted with a rate of 19.6 per cent for the female group above forty years of age, and a rate of 22 per cent for the female senile group.

The peritoneum is an example of a viscus varying with age in its relative frequency as to sex involvement. Thus, although the rate is much higher in the female than the male fetus, the figures are reversed in the group below forty years of age; the figures are, however, reversed again in the group above forty years of age; furthermore, the peritoneum becomes increasingly more involved in the senile female, but less involved in the senile male group.

It is believed that even the few examples given above are sufficient to prove that in any study of the subject of visceral adhesions and bands, both age and sex factors must be carefully considered before any reliable results can be arrived at.

In general, the problem of visceral adhesions may be approached from at least two main points of view. The first, is that of the involvement of the individual viscera by adhesive processes either congenital or acquired; this is the point of view from which Tables I to V inclusive have been considered. The second point of view from which the problem of viscera adhesions may be approached, is that of the actual adhesions themselves. For example, the congenital band frequently found running from the gall-bladder down across the duodenum to the transverse colon, if studied from the first point of view, would be considered under the three separate headings of gall-bladder, duodenum and transverse colon. On the other hand, if studied from the second point of view of the adhesive process itself, this congenital band would be considered as a single distinct structure. It is from this second point of view that Tables

VI, VII, and VIII approach the subject of visceral adhesions, from three particular angles.

The object of Table VI is to indicate the surprising increase in the average number of viscera involved by adhesions with increasing age, in both sexes. It will be seen that below the age of forty the average number of viscera involved does not exceed 4 per case, whereas above the age of forty the average rate of involvement is nearer 5 than 4 per case. Reducing this question to percentage

NO. OF CASES	NO. OF OBS.	AGE	SEX	AVERAGE NUMBER OF VISCERA INVOLVED	INCREASE OVER FOETAL RATE PERCENTAGE
18	58	FOETAL	MALE	3.2	
16	47		FEMALE	2.9	
88	284	BELOW 40	MALE	3.2	NONE
61	181		FEMALE	3.0	3.4
92	424	ABOVE 40	MALE	4.6	43.8
56	248		FEMALE	4.4	51.7
17	81	SENILE	MALE	4.8	50.0
18	83		FEMALE	4.6	58.7

TABLE VI.—Average number of viscera involved by adhesionsi n relation to sex and age.

increase above the fetal rate of involvement, it is shown that whereas there is practically no percentage increase below the age of forty, the increase after this age averages about 50 per cent for both sexes. It is difficult to explain this striking 50 per cent increase on any other basis than that of some increasing degenerative tendency to adhesions, possibly based upon decreased resistance to the irritative and infective trauma to which all viscera are exposed in varying and progressive degrees at all ages in both sexes.

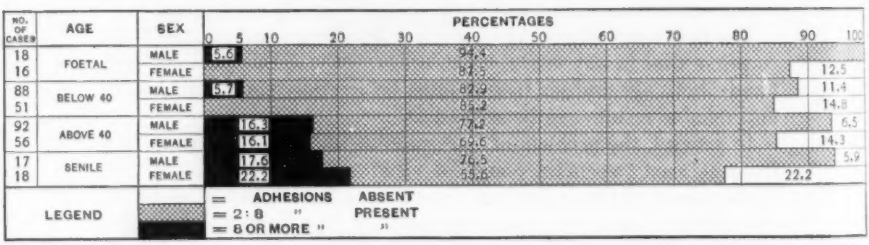
NO. OF CASES
AGE
SEX
PERCENTAGES
0 5 10 20 30 40 50 60 70 80 90 100
18 FOETAL MALE 5.6 94.4
16 FEMALE 87.5 12.5
88 BELOW 40 MALE 5.7 82.9 11.4
51 FEMALE 85.2 14.8
92 ABOVE 40 MALE 16.3 77.2 6.5
56 FEMALE 16.1 69.6 14.3
17 SENILE MALE 17.6 76.5 5.9
18 FEMALE 22.2 55.6 22.2
LEGEND
= ADHESIONS ABSENT
= 2:8 " PRESENT
= 8 OR MORE "

TABLE VII.—Variation in complexity of adhesions present in relation to sex and age.

The relation of age to the complexity of adhesions or the number of viscera involved in any single adhesive process is clearly shown in Table VII. From this one learns that the adhesions found in the fetus are relatively uncomplicated in character, and that complexity is practically a synonym for age. In other words, the increasing complexity of adhesions with age seems to be an indication of the decreasing resistance of the viscera to the trauma of all kinds to which they are subjected throughout life.

It has been shown in Tables VI and VII that the age of forty is critical in relation to the average number of viscera involved, and in relation to the complexity of the adhesions themselves. A study of Table VIII leads to the conclusion that the total variety of adhesions present in any age group also increases with age, but that the marked increase occurs in the thirty–forty-year decade, or ten years before the onset of the two other age changes just referred to.

In summarizing these various age changes, it may be said that the distinguishing characteristics of such congenital or developmental adhesions as are found in the fetus are firstly, the limited average number of viscera involved, and secondly the simplicity and absence of variety in type of the adhesions themselves. The acquired and degenerative adhesions of age, are on the contrary characterized

NO. OF CASES	NO. OF OBS.	AGE	SEX	ACTUAL NUMBER OF DIFFERERENT ADHESIONS PRESENT (0 5 10 15 20 25)
18	58	FOETAL	MALE	10
16	47		FEMALE	8
10	26	BIRTH-2 YRS.	MALE	8
8	16		FEMALE	5
12	30	2–10	MALE	10
11	30		FEMALE	9
11	36	10–20	MALE	10
1	2		FEMALE	1
13	48	20–30	MALE	11
11	38		FEMALE	11
24	86	30–40	MALE	20
14	48		FEMALE	15
23	104	40–50	MALE	23
16	77		FEMALE	18
31	142	50–60	MALE	23
15	59		FEMALE	14
21	97	60–70	MALE	20
7	29		FEMALE	8
17	81	70–80	MALE	19
18	83		FEMALE	25

TABLE VIII.—Total number of variations in types of adhesions present in relation to sex and age.

by the large average number of viscera involved in any given process, the great increase in the variety of adhesions found, and the strikingly increased complexity of the adhesions themselves.

Conclusions. 1. The transverse colon is more frequently involved by adhesions than any other abdominal viscus. Seven women and 8 men out of every 10 persons presumably have some involvement of this viscus by congenital or acquired adhesions. Next in order of frequency of involvement come the gall-bladder, duodenum, peritoneum, omentum, ascending colon, hepatic flexure, appendix, liver and descending colon.

2. Within a range of variation not usually exceeding 10 per cent, the rate of involvement of a given viscus may be greater in the male or in the female, and this relative rate of involvement with regard to sex may further vary with age.

3. The rate of involvement by adhesions, is for several viscera higher in the fetus than at later ages, as for the transverse colon in the male and the terminal ileum in the female.

4. The rate of involvement by adhesions increases rapidly with progressive age for certain other viscera, as for the sigmoid flexure in the male and the adnexa in the female.

5. The age of forty is critical in both sexes with reference to the average number of viscera involved by adhesions in any given case. After the age of forty, there is a sudden increase of involvement by about 50 per cent in both sexes, the increase being somewhat more marked in the male than in the female.

6. Complexity is practically a synonym for age, with regard to the number of viscera involved in any given adhesive process. This increase in complexity amounts to over 200 per cent after forty years of age.

7. Variety in the character of the adhesions present also increases with age. A sudden marked increase of nearly 100 per cent occurs in the thirty–forty-year decade, or ten years earlier than the onset of the marked increase with regard to the average number of viscera involved, and the onset of the increase in the complexity of the adhesions themselves.

8. The distinguishing characteristics of congenital or developmental adhesions, are simplicity and lack of variety in type.

9. The distinguishing characteristics of acquired adhesions, are complexity and variety in type.

IS THE STOMACH A FOCUS OF INFECTION?

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The relation of focal infection to systemic disease, and more particularly to the psychoses, has been the subject of considerable controversy. Before establishing that a focus of infection is the etiologic factor in a systemic disease or in a psychosis, it must first be proven that the bacteria in any organ involved are not merely fortuitous but actually constitute a focus of infection. Periapical abscesses and tonsil infections are generally conceded to belong to the latter category. However, the question is at once raised whether the stomach is a focus of infection in the same sense. The present investigation is concerned with a critical analysis of the relevant facts, as determined by the Rehfuss method of fractional gastric analysis, and the writer wishes to emphasize that there is

no attempt made to discuss whether or not the stomach is a focus of infection when other criteria are employed.

It has been quite generally recognized that acidity is the most important factor in influencing the bacterial content of the stomach. That is to say, the higher the acidity the fewer the numbers and types of bacteria present. The fractional method of gastric analysis makes possible a bacteriologic study of the stomach, which includes not only the active cycle of digestion but the resting phase as well. So far as could be ascertained no quantitative bacterial studies employing this method have heretofore been reported. In fact very little data concerning the types of bacteria in the stomach at different stages of digestion have appeared in the literature beyond the work of Cotton.[1] He claims that: "The stomach and duodenum are very frequently the seat of secondary foci. . . . The bacteria invade the stomach wall and appear to interfere with the secretion of hydrochloric acid, so necessary to digestion. Cultures of the stomach contents will reveal the presence of various types of streptococci and frequently of various types of colon bacilli. The chemical examination of the stomach contents will show either a very low secretion of hydrochloric acid, or, in many cases, its entire absence during the test meal." Upon the administration of autogenous vaccines the acidity of the stomach is increased and the bacteria disappear.

The first criticism which can be advanced against such a position is that these conclusions are based upon single determinations by the Rehfuss method of fractional analysis. The writer has shown[2] that repeated analyses carried out on the same individual within a short period of time yield different acidity curves. In other words the same subject may show a low, high and intermediate acidity on three separate analyses carried out within a single week. This holds true likewise for the average fasting contents. Obviously therefore, it is not valid to base any conclusions on a single determination. Before entering into a discussion of further objections, it would be more appropriate to present the data upon which they are based.

Bacteriologic studies of fractional gastric analyses carried out repeatedly on psychotic patients and normal individuals have shown that in only one-half the instances was there any correlation between high acidity and low bacterial numbers or *vice versa*. In other words there was evidently still another factor operating which precluded any such simple explanation as that wherein acidity alone determined the bacterial count of the stomach. Upon

[1] The Defective Delinquent and the Insane, Princeton University Press, p. 201. New York Med. Jour., 1920, **111**, 672, 721, 770.

[2] Kopeloff, Nicholas: Individual Variation as Influencing the Rehfuss Fractional Method of Gastric Analysis, Jour. Am. Med. Assn., 1922, **78**, 404.

close observation it became apparent that the amount of saliva swallowed by a patient during the two-and-one-half hour period necessary for the complete gastric analysis by the fractional method was of considerable significance. For example, the bacterial counts made on all the gastric fractions varied from 0 up to 100,000 per cubic centimeter, depending upon the individual. Only one patient consistently showed a complete absence of bacteria on repeated analyses. It is of particular interest that this was a case of profound depression. In fact, she refused food and often fasted for as much as forty-eight hours at a time. It is furthermore of importance to note that her secretory activity was greatly reduced. Her mouth was usually exceedingly dry, and it was difficult to stimulate any flow of saliva. The conclusion, therefore, was that the absence of saliva was the limiting factor, so far as her bacterial content was concerned. It might perhaps be mentioned in passing that her gastric acidity was not abnormally high.

The major problem under investigation, namely, the relation of focal infection to the psychoses, demands a thorough investigation of the gastrointestinal tract in order to establish whether or not it is to be considered a focus of infection. Obviously it is essential to determine whether the bacterial flora, and especially the pathogenic members thereof, are true stomach bacteria in the same sense that some abnormal condition in the stomach permits of their presence and consequent multiplication; or whether this flora is a natural resultant of such comparatively external factors as food and saliva.

It is manifestly impossible completely to prevent the swallowing of all saliva during the course of a fractional gastric analysis, in order to determine its relative value as a factor influencing the bacterial content of the stomach. The method finally devised however, proved effective in reducing the swallowing of saliva to a minimum. The procedure consisted in placing an ordinary dental suction tube, which was attached to a running-water vacuum pump, in the subject's mouth throughout the analysis. The subject was continually reminded to move this tube freely about in the mouth (*cavum oris*) and also to expectorate as frequently as possible. In order to reduce the large amount of saliva necessarily swallowed when the Rehfuss tube is introduced, the dental suction tube was kept in the mouth for one-half hour prior to the swallowing of the Rehfuss tube. An added precaution was to have the subjects brush their teeth with particular care and rinse with chlorazene solution the night before and morning of the analysis; the mouth was again rinsed with chlorazene solution followed by successive portions of sterile water before the aseptic dental tube was inserted. The standard Ewald test meal consisted of 35 gm. of sterilized toast and 250 cc of sterile tea. The Rehfuss

tube and syringe were sterilized as well as the test-tubes in which the samples were collected. The attempt therefore was made to have all conditions as aseptic as the circumstances would permit. In this way counts made on the bacteria would be a true approximation of the numbers and kinds actually present in the stomach and could be satisfactorily compared with previous results obtained where saliva was present in greater amount. The acidity of each fraction was obtained by titration, using methyl orange and phenolthalein as indicators, while the hydrogen ion concentration was determined colorimetrically, using the Clark and Lubs indicators. One cubic centimeter of each fraction was plated in triplicate at once upon withdrawal, on both glucose meat-infusion agar and lactose meat-infusion agar, to which brom-cresol purple was added. Since the subjects were not in bed during these analyses, as is customarily the case, but sat upright in chairs, their stomachs emptied in somewhat less than the usual time.

In Table I are presented the bacteriologic and chemical results obtained with a psychotic patient (diagnosed manic-depressive:

TABLE I.—COMPARISON OF GASTRIC FRACTIONS WITH SALIVA REMOVED AND NOT REMOVED—MANIC SUBJECT.

M. Sl.	Saliva not removed.			Saliva not removed.			Saliva removed.		
	Bact. per 1 cc.	TA.	p^H.	Bact. per 1 cc.	TA.	p^H.	Bact. per 1 cc.	TA.	p^H.
F.C. . . .	15,500	5	2.8	...	...	...	2	12	2.8
¼ hour . .	380	11	2.7	310	35	2.9	5	23	2.5
½ " . .	78	41	2.2	5100	37	3.0	8	52	1.7
¾ " . .	5	46	1.8	925	41	2.8	2	70	1.4
1 " . .	60	25	2.5	2800	28	3.0	0	71	1.3
1¼ hours . .	800	18	2.7	110	36	2.2	1	42	1.5
1½ " . .	215	25	2.3	95	43	1.9	1	29	1.7
1¾ " . .	55	6	2.7	12	45	1.8	32	12	2.0
2 " . .	110	28	2.7	5400	10	3.7	*	2	3.0
2¼ " . .	48,000	9	2.7	3200	9	4.3	*		
2½ " . .	46,000	10	2.7	6800	16	3.5	*		

TA., total acidity; p^H., hydrogen-ion concentration (inverse); F.C., fasting contents; * stomach empty.

manic). The first two main headings, "Saliva NOT Removed," are for the fractional gastric analyses carried out at two different times with the technic employed in previous work.[2] Under the final heading, "Saliva REMOVED," appear the data obtained with the modified technic herein described. In the first column of figures giving bacteria per cubic centimeter, where saliva was not removed, we see that the fasting contents contained 15,500 bacteria per cubic centimeter. During the process of digestion the numbers are considerably lower until two and one-quarter

hours have elapsed, when there is a tremendous increase. It may be mentioned, parenthetically, that the unsterilized toast usually given contained an average of about 600,000 microörganisms per gram. The acidity in the stomach is generally sufficient to decimate a large proportion of the original number of bacteria ingested, which would be approximately 50,000 per cubic centimeter of total gastric contents. In the second column of bacterial numbers the fasting contents were unfortunately not obtained, but the remaining figures, while higher than those in the first column, have much the same general proportions, namely, the last few fractions show the highest bacterial counts. Contrast these two columns with the column of bacterial figures where saliva *was removed*. Here the first number is 2 and the last, which is the highest, is 32. The results speak for themselves. In other words, based on the last fraction in the first column where saliva was removed, this represents only 0.007 per cent of the bacteria found in the former fraction. Such a striking reduction makes the conclusion irresistible, namely, that bacterial numbers in the stomach at any one time depend almost entirely upon the saliva swallowed (where the bacterial content of the food may be disregarded).

Several other interesting points may also be noted. The most important of these bears on the relation of the active digestive cycle to the interdigestive phase. In other words it would naturally be expected that the greatest multiplication of bacteria and maximum numbers would be attained in the "interdigestive" phase when the stomach is relatively at rest and the secretion of acid is at a minimum. Accordingly, therefore, the fasting contents should show the highest bacterial count. But such is not the case. As a matter of fact the last fractions, whether saliva be removed or not, contain a far greater number of bacteria. Unquestionably the secretion of acid during the actual process of digestion, together with the natural motility of the stomach, should materially reduce the numbers present at the outset. Contrary to this inference the numbers are actually increased, and this is additional evidence that the continual swallowing of saliva (which contains millions of bacteria per cubic centimeter) is in reality the factor which determines the bacterial content of the stomach. The mere act of swallowing the Rehfuss tube is alone responsible for carrying down considerable saliva, and this is probably why the bacterial count on the fasting contents is as high as it is. Furthermore, it has been observed that toward the end of the analysis, when the stomach is almost empty, it becomes necessary to manipulate the tube considerably in order to obtain the fraction, and therefore a large increase in bacterial numbers would naturally accompany this procedure. Occasionally it will be found necessary to manipulate the tube during some stage of the analysis, which almost invariably results in an increase in the number of

bacteria. Again, the fact that the bacterial numbers where saliva was removed were so small as to be negligible is significant when it is noted that the secretion of acid is without much influence, *i. e.*, only two bacteria appear where the total acidity is as low as 12 and as high as 70. All these considerations mentioned point to the fact that the saliva is the most important single factor in influencing the bacterial content of the stomach under the conditions employed. No attempt is made here to underestimate the importance of gastric acidity in influencing the numbers and kinds of bacteria. If anything, these data corroborate from another aspect the bacteriologic findings of previous investigators who claim that gastric acidity is sufficient to control the development of bacteria in the stomach. There are two important factors to be considered in this connection: (*a*) the actual concentration of hydrogen ions and buffer salts, and (*b*) the element of time. Bacteriologic studies which have been concerned with mathematical aspects bring out this latter point very clearly. In other words, while it is possible to find a great number of bacteria in the stomach at one particular moment, the continued limiting effects of acidity will soon be manifest, and it will be seen that in only very few cases, and chiefly where organic lesions are present, may the stomach be regarded as a focus of infection. However at any particular time it is possible to find numbers of bacteria, and it is the contention borne out by these data that at such time the saliva is the more important factor. It is scarcely necessary to add that the finding of bacteria may or may not be of significance, depending upon the numbers and types found; still it is generally conceded that large numbers would be expected in such stomachs as might be considered foci of infection.

TABLE II.—COMPARISON OF GASTRIC FRACTIONS WITH SALIVA REMOVED AND NOT REMOVED—NORMAL SUBJECT.

S. My.	Saliva not removed.			Saliva not removed.			Saliva removed.		
	Bact. per 1 cc.	TA.	p^H.	Bact. per 1 cc.	TA.	p^H.	Bact. per 1 cc.	TA.	p^H.
F.C. . . .	7,000	15	3.0	12,000	20	2.7	97	14	3.0
½ hour . .	1,050	17	3.0	550	25	2.6	300	16	3.0
½ " . . .	700	30	2.8	1,700	39	2.6	40	22	2.4
¾ " . . .	780	42	2.7	1,400	62	1.6	180	38	1.9
1 " . . .	1,000	50	2.6	1,800	76	1.6	138	45	1.7
1½ hours . .	1,050	37	2.6	1,100	73	1.5	115	49	1.7
1½ " . .	250	39	2.3	600	65	1.4	38	52	1.7
1¾ " . .	450	47	1.6	800	45	1.6	43	49	1.7
2 " . .	750	25	2.1	1,000	22	2.4	70	35	1.8
2¼ " . .	31,000	7	4.5	600	21	2.4	300	15	4.2
2½ " . .	58,000	4	5.0	900	30	1.9	*	7	4.4

TA. total acidity; p^H, hydrogen-ion concentration (inverse); F.C., fasting contents; Bact., bacteria; * stomach empty.

In Table II are given the results obtained on a healthy normal individual, in order to show clearly that the mental condition did not unduly affect the conclusion previously arrived at. Here, again, are seen practically the same points as were brought out in the previous case. Thus where saliva is not removed, as in the first column, the fasting contents contain 7000 bacteria per cubic centimeter while the last two fractions contain 31,000 and 58,000 bacteria per cubic centimeter respectively. The intermediate fractions vary between 250 and 1050 bacteria per cubic centimeter. In the second column of bacterial numbers, where saliva was not removed, there is a variation from 550 to 12,000 bacteria per cubic centimeter. Comparing this with the third column, where saliva *was removed*, a striking decrease is evident. There is a variation from 38 to 300 bacteria per cubic centimeter. In other words, the *highest* bacterial count where saliva was removed is lower than the *lowest* bacterial count in the second column where saliva was not removed, and very slightly higher than the lowest bacterial count in the first column where saliva was not removed. The conclusion is therefore corroborated that the saliva is one of the most important single factors influencing the bacterial content of the stomach. In the first column where saliva is not removed, as with the previous subject, it is seen that the bacterial count for the fasting contents is lower than in the last two fractions, showing that there could not have been any multiplication of bacteria in the interdigestive phase. The same fact may be observed in the final column where saliva was removed. The second column is an exception to the rule, but may easily be explained on the basis that somewhat more saliva was swallowed with the Rehfuss tube than is ordinarily the case. It is furthermore obvious that there is no correlation between bacterial numbers and variation in acidity as measured either by titration or hydrogen-ion concentration, which points to the greater importance of saliva as a limiting factor.

Similar results were obtained with other psychotic patients (also manic-depressive: manic). It is scarcely necessary to discuss these results in detail, since the data which corroborate the points already emphasized are published elsewhere.[3]

An important consideration, however, is that these patients had a very low acidity and would be precisely the type of subjects therefore in which bacteria might gain a foothold and make the stomach a focus of infection. Judging from the results when saliva is removed such is far from being the case.

It must be remembered that a fractional gastric analysis carried out on a normal individual is one thing and when carried out on

[3] Kopeloff, Nicholas: The Fractional Method of Gastric Analysis as Applied to the Psychoses, State Hospital Quarterly (New York), 1922, **7**, 326.

a manic patient is quite another. The difficulties must truly be seen to be appreciated. The continual conversation must perforce induce a series of swallowing reflexes, which tend to carry saliva down the esophagus despite any devices for removal of saliva. The attempt, therefore, to remove saliva during the course of analysis on such a patient could scarcely be put to a severer test or meet with less response. Consequently the data take on an added significance when they so definitely point to the observation that the removal of saliva is accompanied by a striking reduction in bacterial count. The conclusion, therefore, is that saliva influences the bacterial content of the stomach.

A qualitative study of the types of bacteria found in the saliva, and by the fractional method of analysis, in the stomach serves as additional evidence in support of these findings.[3] The organisms found most frequently have been streptococci, yeasts, staphylococci, members of the lactic-acid and aërogenes groups. It was found that there was no correlation between the degree of acidity and the species or numbers of bacteria found. Streptococci were associated as frequently with stomachs having high acidity as with those having low acidity. The toast contained many yeasts and some bacteria. The other bacteria noted were almost invariably to be found in the saliva, so that there remains no question but that the bacterial flora of the stomach is a resultant of purely external factors, food and saliva.

Therefore, Cotton's[1] contention that the stomach is a focus of infection finds no substantiation after a critical inspection of the fundamental facts. His conclusions are based upon results obtained by the Rehfuss method, and therefore are open to the following objections: (*a*) Repeated analyses by the Rehfuss method on the same individual yield different curves and little constancy in bacterial species; (*b*) no correlation can be established between low acidity and high bacterial numbers or species, since it has been shown that acidity is not the limiting factor in determining the bacterial content of the stomach during a fractional analysis by the Rehfuss method (*c*) saliva is the most important factor in influencing the bacterial content of the stomach (without gastric lesions), although the bacterial content of the food ingested must be considered.

Should the objection be raised that the bacterial content of the stomach is an academic one, the burden of proof falls on him who asserts that it is possible to determine infection in the lining of the stomach wall. Removal of the stomach is the only positive method yet known of proving whether or not such infection exists. The advantage of obtaining the knowledge in such a manner could scarcely be considered worth while from the standpoint of treatment. Therefore, infection in the stomach (without lesions) has been diagnosed by Cotton from results obtained by the Rehfuss

method. Two possibilities are open: The first is that the infection is secondary and has been brought by means of the blood stream and lymph channels, and the second is that it results from the swallowing of infected material. In either event if the infection is "hidden" in the living stomach wall, the gastric contents upon withdrawal will not show the bacteria in question. On the other hand, if the bacteria from the focus are being actively discharged into the stomach contents, then if the infection has come by way of the blood or lymph stream the number of bacteria found in the gastric contents should not be decreased by cutting off the flow of saliva. However, such is not the case, and it has been shown that the removal of saliva reduces the bacterial content. Consequently it must be inferred that the bacteria in the gastric contents are introduced by the swallowing of saliva. It naturally follows then that there should be a multiplication of microörganisms when the stomach is at rest. However, it has been previously shown[2] that no such multiplication exists even in stomachs having a low acidity. No question is raised here with regard to the stomach being a focus of infection where organic lesions are present, for undoubtedly ulcers and other similar conditions may well act as foci of infection. The chief concern is whether the stomach is a focus of infection where there is no indication of organic lesions, or where no other criteria than the Rehfuss method for establishing such infection has been used, as in cases reported by Cotton,[1] which have yielded to treatment with autogenous vaccines. Since the bacterial flora of the stomach have been shown in this paper to be the resultant of external factors, such as food and saliva, the results obtained by the Rehfuss method of fractional gastric analysis cannot be considered adequate criteria for determining whether or not the stomach is a focus of infection. Consequently no validity can be attached to the conclusion based upon the use of this method that the stomach bears an etiologic relationship to the development of systemic disease or a pyschosis.* Studies concerning the presence and elimination of foci of infection (teeth and tonsils) in psychoses are now in progress, and in the near future a report will be made on a group of functional psychoses all showing infected teeth and tonsils. In one-half of the group the foci of infection were removed, the remaining half of the group were not operated upon and therefore could be regarded as "controls."

The staff have been very generous in their assistance, particularly Dr. C. O. Cheney, and Mr. E. J. Kennedy has rendered invaluable aid in the laboratory.

Summary. 1. A quantitative as well as a qualitative study was made of the bacteria found in the stomach at different stages

* N. Kopeloff and C. O. Cheney.: Studies in Focal Infection; Its Presence and Elimination in the Functional Psychoses. Am. Jour. Psychiatry, Oct., 1922.

in the digestive process, employing the fractional method of gastric analysis.

2. The device used for the removal of saliva during gastric analysis was a dental suction tube. This made possible a comparison of gastric fractions contaminated and uncontaminated by saliva.

3. Bacterial counts showed a striking reduction in numbers in gastric fractions when saliva was inaccessible. The highest number of bacteria per cubic centimeter in a psychotic patient (manic-depressive: manic) where saliva was *not* removed was 48,000; where saliva *was* removed the highest number found was 32. Similar results were obtained with a normal individual and with other manic patients.

4. These data take on an added significance when it is remembered that the swallowing of saliva is particularly difficult to control in manic patients. Furthermore it is important to note that this reduction in numbers of bacteria when saliva is removed occurs alike with patients having a very low gastric acidity and those of a more normal type.

5. There is no correlation between high acidity in the stomach and low bacterial numbers, or *vice versa*. Streptococci were found associated with high as often as with low gastric acidity, consequently there seems to be no reason to attach undue importance to their presence or therefore to consider the stomach a focus of infection. This means that another factor, the saliva, is of greater importance in determining the bacterial content within certain limits.

6. The fact that the bacterial count on the "fasting contents" is usually considerably lower than during the process of digestion indicates that little or no multiplication of bacteria takes place when the stomach is relatively at rest.

7. The microörganisms found in the different gastric fractions with greatest frequency are: Yeasts, staphylococci, streptococci and members of the lactic-acid and aërogenes groups. Almost invariably these are found in the saliva of the same patient or in the food given. Consequently they cannot be regarded as constituting a true bacterial flora of the normal stomach.

8. From these various considerations it may be inferred that the stomach is not acting as a focus of infection but merely as a receptacle for the bacteria poured into it. This is in agreement with the bacteriologic investigations of others to the effect that gastric acidity is sufficient to prevent bacterial development.

Conclusion. The bacterial content of the stomach is influenced by the saliva. The Rehfuss method of fractional gastric analysis cannot be considered an adequate criterion in determining whether the stomach is a focus of infection.

REVIEWS.

A Dictionary of Dental Science. By L. Pierce Anthony, D.D.S., Associate Editor of the *Dental Cosmos*. Pp. 324; 23 plates. Philadelphia and New York: Lea & Febiger, 1922.

The author's long experience in dental literary work has well fitted him to produce this, as far as we know, the first purely dental dictionary in the English language. The book defines all words likely to be met by the dentist in medical works of interest to him, and in addition many technical dental words are found that are not included in medical dictionaries. In view of the ever-increasing contact between the two professions the book should be valuable for the physician as well as the dentist. I.

Pulmonary Tuberculosis. By Maurice Fishberg, M.D., Clinical Professor of Medicine, University and Bellevue Hospital Medical College; Chief of the Tuberculosis Service, Montefiore Hospital for Chronic Diseases, and of Bedford Hill Sanatorium for Incipient Tuberculosis. Third edition, revised and enlarged. Pp. 891; 129 engravings and 28 plates. Philadelphia and New York: Lea & Febiger.

Books descriptive of a single disease are so frequently written by a specialist with the object of exploiting some special views or method of treatment, that they are generally viewed with suspicion by the general practitioner. Unfortunately many works on tuberculosis devote too much space to one phase of the disease, while other equally important aspects are treated briefly and casually. This too-frequent failing has been avoided in the third edition of this unusually well-balanced work, which has been improved by the addition of several chapters dealing with certain phases of this disease frequently disregarded, while the other chapters have been largely rewritten or amplified so as to present the more recent views and researches. While it is impossible to agree fully with all the views of this author, there is no recent work which presents the subject of tuberculosis in such a convenient form, from such a sane viewpoint, and at the same time contains so much information of equal value to the general practitioner and to those physicians who are specially interested in this disease. C.

MODERN METHODS IN THE DIAGNOSIS AND TREATMENT OF RENAL DISEASE. By HUGH MACLEAN, M.D., D.Sc., Professor of Medicine, University of London and Director of the Medical Clinic, St. Thomas's Hospital. Pp. 102; 4 illustrations. Philadelphia and New York: Lea & Febiger, 1922.

To those of the medical profession interested in the study of kidney disease no more thorough and comprehensive volume of its size has been placed before the reader. Concentrated in a comparatively few pages are all the important facts that have to do with the diagnosis and treatment of renal disease. This concentration of the subject matter is of particular value to the practitioner because in the past few years in many ways our conception of nephritides has very materially changed and many new studies have appeared which have to do with the determination of the function of the kidneys. The author deals with first the chief functions of the kidney, then goes on and discusses the kidney in disease, the significance of albumin and casts, blood examinations and other tests to determine renal function. He describes the proper examination of patients to determine renal inefficiency and has a series of illustrative cases. He also writes upon the importance of determining the condition of the kidney in certain surgical lesions and concludes with some observations on the dietetic treatment of nephritis. All these phases of urinary pathology and diagnosis are treated most sensibly. The book is well rounded out, well proportioned and can be heartily recommended to the practitioner of medicine. M.

ADVANCED SUGGESTION. By HAYDN BROWN, L.R.C.P. (EDIN.), F.R.S.M. Pp. 402. New York: William Wood & Company, 1922.

THIS is the second edition, a review of the first one having appeared in this journal a few years ago. Inasmuch as there have been very slight changes, with the exception of the addition of three chapters, the original review is herewith reprinted.

"On page 230, in a chapter on 'A Study in Morbid Growths,' appears the following paragraph: 'I have myself, at will—knowing how to act and what to expect—obtained unquestionable results by psychotherapy in dealing with examples of organic disease and abnormal growth, which could not be exceeded by radium in similar cases.'

"On the next page, paragraph 8 reads as follows: 'I have indisputable proof of organic disorder and the development of newgrowth having been originated by suggestion. In one such case I have reversed the causative impression, and the newgrowth has regressed and disappeared.'

"A further reading of this chapter denotes that the author has the belief that cancer can be cured by psychotherapy, or, as he calls it, neuroinduction. He prefers the latter to suggestion, for neuroinduction to him implies 'the accurate conveyance of reliable sensations and conclusions, and their correct interpretation; it is a true sense demonstration and elucidation, both physically and mentally.'

"The author in his introduction to the chapter 'Study in Morbid Growths,' which contains the paragraphs mentioned above, makes the following naïve statement: 'I wrote the following eight and a half pages some time before finishing this book and I offered it to two of the leading medical journals. It was declined—for what reason I shall probably never know; but I can only think, in all charitableness of heart, that the time was not ripe for it.' He later mentions specifically the *British Medical Journal* as one journal which refused to publish his views.

"It is hardly necessary to say any more about this book on *Advanced Suggestion*. The astonishing part is that such a work as this should be put on the market by a reputable publisher and that the author is a Fellow of the Royal Society of Medicine."

A further surprising fact is that this book has reached its second edition, from which it is a justifiable conclusion that the medical public will buy anything that appears in book form.

TREATMENT OF INJURIES OF THE PERIPHERAL SPINAL NERVES. By SIR HAROLD J. STILES, K.B.E., F.R.C.S. (EDIN.), Regius Professor of Clinical Surgery, University of Edinburgh; and M. F. FORRESTER-BROWN, M.S., M.D., formerly Surgeon, Edinburgh War Hospital. Pp. 178; 67 illustrations, of which 33 are in color. Oxford Medical Publications, 1922.

THIS monograph has as its object "to place at the disposal of the general surgeon who may be called upon to deal with an occasional case of peripheral nerve injury, the experience which has been gathered from the exceptionally abundant material provided by the Great War." The authors have had an unusually large experience in this field of work and in this book attain their object. It cannot be looked upon as an exhaustive treatise on the subject nor has it been intended to be. The reviewer has no criticism to offer of either the text or the illustrations, both of which are good. Undoubtedly, the general surgeon may find himself in a position of having to do peripheral nerve surgery, in which event he will find this book useful. The reviewer believes, however, that the general surgeon is not the one to do this work if others are available who have made a special study of neurologic surgery. Peripheral nerves are in reality prolongations of the central nervous sys-

tem, and it requires more than written directions to handle its lesions properly. The reviewer was pleased to see the stress laid upon anatomy in this monograph. It is unquestionably true that the surgery of lesions of the peripheral nerves require an exact knowledge of the anatomy of the part in question. It is hoped that we will soon begin to hear of the end-results of the various operative procedures used in treating nerve injuries, especially in the Great War. Then will we really learn the value of each procedure. R.

De Arte Phisicali et de Cirurgia of Master John Arderne, Surgeon of Newark. Dated 1412. Translated by Sir D'Arcy Power, K.B.E., M.B. (Oxford), F.R.C.S.; from a transcript made by Eric Millar, M.A. (Oxford). Pp. 60; 14 illustrations. New York: William Wood & Company, 1922.

Master John Arderne, of Newark, was born in 1307, and became an operating surgeon, whose practice lay among the nobility, wealthy landowners and the higher clergy. He was a sound, practical surgeon and taught that wounds should heal without suppuration. He cut boldly and invented the operation for the cure of fistula, which, after falling into disuse for nearly five hundred years, is now universally employed. His medical treatment, on the other hand, was that of his time, employing spells, herbs and nasty or innocuous substances. The present work consists of a photographic reproduction of an illustrated manuscript of Arderne's works, with a translation and notes by Sir D'Arcy Power. The illustrations are very quaint and the many medicinal treatments are amazing; the surgical sections are of much greater interest.

As the first research study in medical history of the Wellcome Historical Medical Museum, the book should be well received and should be of value to those interested in early surgery and in the history of medicine. P.

Aids to Bacteriology. By William Partridge. Fourth edition. Pp. 276. New York: William Wood & Company, 1922.

In this new edition the author has made many additions, bringing his book well abreast of the times. Preparations of more recent media have been incorporated and the H-ion method of titration is suggested, but the reader is referred to other sources for its technic.

The different typhoid vaccines and the Dreyer agglutination test have been added to the section on typhoid; and the anaërobes have been brought up to date by the inclusion of those isolated from

wounds and soil during the war, with comments on wound antiseptics. Among the filtrable viruses, additions have been made to the foot-and-mouth disease, trench fever and typhus fever—also the Proteus X-9 agglutination test. The fermentation reactions of the common yeasts have been tabulated.

In all, the book must be considered as a manual. As such, it will be of assistance to the laboratory diagnostician in the determination of pathogenic bacteria—Trichomycetes, Blastomycetes, Hyphomycetes and Protozoa alike. J.

MANUAL OF PHYSIOTHERAPEUTICS. By THOMAS DAVEY LUKE, formerly Physician, Peebles Hydropathic, Peebles, N. B.; Assistant Physician, Smedley's Hydropathic, Matlock; some time lecturer at the Edinburgh University. Second edition. Pp. 480; 210 illustrations. New York: William Wood & Company, 1922.

THIS work is a revised edition of the author's *Manual of Natural Therapy*, published in 1908. The practitioner will here find adequate descriptions of the theory and technic of therapy by means of heat, light, baths, massage, electricity and other physical agents. The fundamental defect of the work—shared by the majority of books and papers upon this subject—consists in the too ready acceptance of unproved dicta. Indeed there is probably no field in medicine which more richly deserves a thoroughgoing investigation from the standpoint of modern physiology than the field of physiotherapy, and until such an investigation is forthcoming we need feel no surprise that the claims of the osteopath and chiropractor remain unrefuted in the public mind. However, despite the fact that in reading this book one is here and there reminded of these less legitimate schools of therapy, the book, on the whole, is well arranged and compares favorably with other standard works on physiotherapeutics. A.

BASAL METABOLISM: ITS DETERMINATION AND APPLICATION. Edited by FRANK B. SANBORN, M.S. Pp. 282. Boston: Sanborn Company, 1922.

THIS volume is intended to supply physicians and technicians with a reference book that will be a guide in making basal metabolism tests and in interpreting the same. The editor has prepared some original articles which deal with the fundamental principles while the remainder of the book consists of compilations of abstracts

and original papers by various authors, each dealing with a different phase of the subject. The result of this is much repetition.

A description is given of the various types of indirect calorimeters, without comment on the merits of each type. It seems to the reviewer that a few words on the advantages and disadvantages of the open and closed types might have been given and a spirit of impartiality still maintained. This book will find a place with those who wish a digest of this subject without going into the voluminous literature. J.

CANCER OF THE BREAST AND ITS TREATMENT. By H. SAMPSON HANDLEY, M.S., M.D. (LOND.), F.R.C.S. (ENG.), Hunterian Professor of Surgery and Pathology in the Royal College of Surgeons of England; Surgeon to the Middlesex Hospital and to Its Cancer Charity, and Lecturer to Its Medical School. Second edition. Pp. 404; 82 illustrations. New York: Paul B. Hoeber, 1922.

THE present edition contains new chapters on Radiologic Treatment, on Recurrence and Its Operative Treatment, on Paget's Disease of the Nipple, on Lymphangioplasty, and on Injury as a Causative Factor in Carcinoma. Chapter IX has been rewritten.

The work contains, as one would surmise, a complete review of the author's researches on dissemination, which he concludes is proven for cancer of the breast. Should it prove to be true for all the carcinomata, the surgery of malignant disease for the first time is placed upon a rational basis, and a criterion is provided by which variations in surgical technic can be judged.

The importance of pathology in the approach to the operative treatment of cancer is emphasized, for technical work must be guided and checked at every step by a first-hand pathologic knowledge. The type of operation which the author performs, therefore, is based upon such information, and important facts are discussed in planning the skin incision, removal of the permeated area of deep fascia, etc.—all of which are of the utmost importance.

The work is distinctly a review of the author's own ideas and technic. No mention is made of the type of operative procedure successfully carried out by other surgeons, if such procedure does not accord fully with the theory of permeation. He believes roentgen-rays are suitable, especially for prophylactic irradiation, covering a wide area, or for the treatment of multiple scattered deposits in the parietes. Radium should be given the preference if the recurrence is single, or if nodules are only present in one or several limited areas. With all its limitations, radium has secured a definite position in the treatment of breast cancer, relieving pain,

prolonging life, and in single recurrences it presumably may complete the cure of the disease.

The chapter on Lymphangioplasty describes the method of performing this operation, and the benefits, as well as cases suitable for this measure are discussed. The chapter on Injury as a Causative Factor in Carcinoma alludes to many facts of importance from the medicolegal standpoint. S.

PHYSIOLOGY AND BIOCHEMISTRY IN MODERN MEDICINE. By J. J. R. MACLEOD, Professor of Physiology in the University of Toronto; assisted by R. G. PEARCE, A. C. REDFIELD and N. B. TAYLOR and others. Fourth edition. Pp. 992; 243 illustrations. St. Louis: C. V. Mosby Company, 1922.

THE presentation to the public of the fourth edition of the author's well-known text-book follows most appropriately the important work on pancreatic extracts that has recently appeared from his laboratory. One looks eagerly to find if it has been included and is rewarded on pages 713 to 715 with a modest but satisfactory account of "insulin" and its effects.

Important additions have also been made in the section devoted to the circulation of the blood. In the chapters on the electrocardiogram are to be found, in addition to the usual subject-matter, a full description of the "triangle method," Lewis's concept of the "bicardiogram" and the "circus-movement" hypothesis of auricular flutter, the last properly credited to Mines. Space forbids to do more than mention other subjects that have been rewritten, such as the output of the heart, intracardiac pressure, acid-base equilibrium, capillary circulation, etc. Considering that only two years have elapsed since the appearance of the third edition, the authors seem to have amply realized the function of the volume, "To describe not merely what already has been achieved in the clinical applications of physiology, but also to anticipate where this application is likely soon to be made and to prepare the way by describing the physiologic principles that may be involved." In spite of the limitations acknowledged in the preface, one cannot but be surprised at the total omission of a consideration of the special senses, the spleen and other organs of internal secretion.

K.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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AND

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Cardiac Gallop Rhythms.—LeBard (*Arch. d. mal. du cœur*, 1922, 15) contributes an exhaustive study of gallop and triple cardiac rhythm. Acoustic differences between the various types (he recognizes three) are drawn with a fine distinction that is not usually attempted by American clinicians: (I) The presystolic (or mesodiastolic) gallop rhythm of the "nephritic heart" is described as representing not only the gallop sound that occurs shortly before the first heart sound, but others that extend forward into mesodiastole and which may be actually nearer the preceding second sound than the succeeding first sound. The author points out that wherever this sound occurs, however, it is a phenomenon of telediastole. The presystolic gallop is generally believed to be due to auricular contraction. (II) The protosystolic gallop is due, he believes, to a dissociation of the valvular and the muscular elements of the first sound. It is compatible with a long period of compensation and is in this respect different from the presystolic or mesodiastolic gallop, which is an indication *per se* of cardiac strain. The author does not differentiate this type of split first sound from the reduplication that may occur in normal hearts in the erect posture, and does not describe the effect of posture upon this type of gallop. (III) The protodiastolic gallop is rare, but the author has had several instances of it. It differs radically from the first two types, from the clinical point of view, though it resembles the mesodiastolic gallop closely in its acoustic properties. The protodiastolic gallop gives a more powerful, palpable, and sometimes visible, apical

thrust and is associated with jugular collapse; the other types are synchronous with a jugular wave. He presents tracings which show that this type of gallop definitely precedes auricular contraction and is, therefore, a physiologic entity.

The Toxicity and Parasiticidal Action of Arsenicals as Influenced by Their Rate of Excretion.—VOEGTLIN and THOMPSON (*Jour. Pharm. and Exp. Therap.*, 1922, **20**, 85) have studied in albino rats the rate of excretion of three groups of arsenical compounds, the trivalent arsenoxides, arsenobenzene derivatives (the arsphenamin group), and pentavalent arsenicals, and have compared the rates of excretion with the factors of toxicity and parasiticidal action. They find considerable variation in the rate of excretion in different individuals of the same species. The trivalent oxide compounds, which are more toxic and also more active therapeutically, show the slowest rate of excretion; the comparatively nontoxic and therapeutically less active pentavalent compounds are excreted with the greatest rapidity, while the arsenobenzene derivatives occupy an intermediate position. The ratio between urinary and fecal excretion of different drugs shows great variation, from 80 to 90 per cent of the pentavalent compounds being excreted through the urine, while 82 per cent of injected arsphenamin leaves the body through the feces. The authors believe that the evidence indicates that the chemical constitution, in so far as it is responsible for the physical properties of an arsenical, determines its rate of excretion and, therefore, its toxicity and parasiticidal action. In the next paper of the series, VOEGTLIN, DYER and MILLER (*Jour. Pharm. and Exp. Therap.*, 1922, **20**, 129) show that if the removal of arsenicals from the body is prevented, by means of complete ligation of the ureters, bile duct, or both (depending upon the type of drug and its relative urinary and fecal excretion), their toxicity and parasiticidal activity is greatly enhanced. When the ureters alone were ligated this effect was marked only in those drugs chiefly excreted through the kidneys; and in the same way ligation of the bile duct alone caused a great increase in the toxicity and trypanocidal activity of arsphenamin and neoarsphenamin, which are largely excreted in the feces. The authors conclude that their experiments offer direct proof of the theory that the toxicity and therapeutic value of arsenicals is governed by the rate of excretion from the body, and that Ehrlich's chemical theory of organotropism and parasitotropism is disproved. Retention of arsenicals by the tissues of the host is, therefore, a necessary requisite for drugs of practical chemotherapeutic value, but the retention must be followed by such a chemical change, effected by the tissues, as ultimately to lead to the formation of arsenic in a form which can be easily excreted.

The Apparent Role of Immunity in the Genesis of Neurosyphilis.—The present status of our knowledge on this important subject is summed up by KEIDEL (*Jour. Am. Med. Assn.*, 1922, **79**, 874). He points out the applicability to neurosyphilis of the "laws of progression and of inverse proportions," *i. e.*, that various tissue groups are not equally susceptible and reactive to syphilitic infection, and that an inverse quantitative relationship exists in the intensity of consecutive

reactions to infection. Thus, the incidence and gravity of neurologic reaction is regulated by the antecedent tissue reactions in other parts of the body, so that patients who show only mild reactions to early syphilis are more liable to neurosyphilis than those who have severe secondary lesions. The author points out, however, that the influence of natural immune reactions may be greatly altered by the factor of antisyphilitic treatment. It is shown that in early syphilis a short course of intensive treatment predisposes the patient to neurosyphilis while prolonged courses of adequately intensive, continuous treatment greatly reduce the incidence of neurologic damage. Another modifying factor in women is pregnancy, which tends to suppress the lesions of syphilis, particularly neurosyphilis, and to induce latency.

Effects of Antisyphilitic Therapy as Indicated by the Histologic Study of the Cerebral Cortex in Cases of General Paresis.—SOLOMON and TAIT (*Arch. Neur. and Psych.*, 1922, **8**, 341) have had the unusual opportunity of studying histologically the brains of 27 cases of general paresis which had been more or less intensively treated during life. For purposes of comparison, the brains of 15 untreated cases were also studied. So far as parenchymatous, true vascular or neuroglia changes are concerned, no conclusions could be drawn because of the nature of the pathology of these structures in general paresis. The critical finding of diffuse plasma cells in the perivascular and pial infiltration could be fairly accurately compared in the treated and untreated groups. It was found that plasma cells were few and infrequent in most of the treated patients, and this was so uniformly the case that it was often possible to predict from the histologic picture whether or not the patient had been treated. Also both lymphocytic perivascular infiltration and pial infiltration were strikingly less in the treated than in the untreated group. Neither the age of the patient, the clinical variety of the psychosis, its duration, nor the kind and amount of treatment given seemed to have any distinct bearing on the amount of cellular inflammatory reaction. They conclude that antisyphilitic treatment of paretics does affect the histologic picture and that this is probably an evidence of lessened chronicity of the process.

Glucose-tolerance Test.—BEELER, BRYAN, CATHCARD and FITZ (*Jour. Metab. Res.*, 1922, **1**, 549), by the aid of the stomach tube, found that there was great variation in the absorption of glucose ingested for the purpose of determining tolerance. Administration of the glucose intravenously corrected this error, but added to the complication of the procedure. The writers suggest, therefore, that the glucose be administered by mouth, as usual, and that at the end of an hour, the stomach should be completely emptied. The amount of glucose recovered in the stomach contents should be subtracted from the amount originally given and the amount absorbed per kilo body weight thus calculated. Interpretation of the resulting blood-sugar curve may then be based upon a knowledge of the approximate amount of glucose which was able to influence that curve. Other factors of error, such as variation in the speed of absorption from the small intestine and increase of blood volume by absorption of fluid may be safely disregarded.

SURGERY

UNDER THE CHARGE OF

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Recognition of Congenital Syphilitic Inflammation of the Long Bones.—TURNBULL (*Lancet*, 1922, **1**, 1239) believes that syphilis in the fetus or in infants may give rise to inflammation in the diaphysis at a distance from the epiphysis or in the periosteum. Much more commonly, however, it causes inflammation in the diaphysis at its junction with the epiphyseal cartilage; that is to say, in the metaphysis and in the epiphyseal cartilage itself. Congenital syphilitic disease of bone is not a general systemic condition, but is due to the local presence of spirochetes. The older the child, the fewer are the portions of bone affected. In the fetus the infection tends to be widespread, but it is not necessarily universal. The femur, tibia, humerus and ribs are sites of election.

Pyelography.—KIDD (*Brit. Med. Jour.*, 1922, **1**, 748) considers it unwise to try to do both kidneys at one sitting. It is a mistake to employ too large a ureteral catheter. The author makes use of a No. 5½ Charriere. Sterilization of catheters with hot formalin vapor helps to avoid implanting infection in the kidney. It is quite a useless procedure to measure the amount of urine coming away, with the idea that this will give information as to whether the renal pelvis is a large one or a small one and as to how much fluid to inject before taking a picture. This is the bedrock difficulty in pyelography. This method of clinical research is indicated particularly in cases of severe abdominal pain of doubtful origin, to determine the nature of abdominal tumors and to complete the diagnosis in many cases of hematuria and pyuria.

Hyperplasia of the Rudimentary Lymph Nodes of the Prostate.—FUKOSE (*Surg., Gynec. and Obst.*, 1922, **25**, 131) says that small, primitive or rudimentary lymph nodes occur normally throughout the prostate in the form of very small aggregations of lymphocytes located beneath the glandular and duct epithelium, most marked toward the outlets of the ducts. They are analogous to the rudimentary lymph nodes found in other organs as the liver, kidneys, uterus, etc. Hyperplasia of these rudimentary lymph nodes of the prostate occurs chiefly in chronic hyperplastic prostatitis and in primary carcinoma of the prostate. In both conditions the hyperplasia is essentially an inflammatory one, due to chronic infection or irritation and possesses the same significance that such hyperplasiæ have in other parts of the body. In the absence of chronic inflammation a hyperplasia of the

primitive lymph nodes of the prostate occurs in the lymphatic constitution and may be found also in other generalized diseases of the lymphoid system as Hodgkin's disease, lymphocytoma and leukemia. In both the inflammatory and noninflammatory hyperplasias, well-developed germinal centers may be produced in the hyperplastic node. Other evidences of functional activity by these hyperplastic nodes are shown in the metastasis of pigment, tubercle bacilli and carcinoma cells to them.

Malignant Neoplasms of the Extrahepatic Biliary Ducts.—RENSHAW (*Ann. Surg.*, 1922, **76**, 205) says that cancer of the bile ducts as a clinical and pathologic entity was not recognized previous to the middle of the nineteenth century. Malignancy of the bile ducts, while less common than that of the gall-bladder, is not uncommon. The ratio in a series of 104 cases of malignancy of the biliary ducts and gall-bladder was 1 to 4. Carcinoma is the most common type of neoplasm found. Gall stones would seem to be of greater etiologic importance than is generally considered. About two-thirds of the cases occur between the ages of fifty and seventy years. A diagnosis of malignancy of the ducts is uncertain. After a diagnosis of obstructive jaundice has been made exploration is generally advisable. From the standpoint of slowness of growth and rarity of metastasis, surgical treatment should be favorable.

Air Embolism following Various Diagnostic or Therapeutic Procedures in Diseases of the Pleura and the Lung.—SCHLOEPFER (*Johns Hopkins Hosp. Bull.*, September, 1922, p. 321) emphasizes that complications may follow various diagnostic and therapeutic procedures. The sudden release of a great amount of fluid in emaciated people with a neurotic constitution may cause a similar clinical picture. Because of its slightness and short duration with lack of localized cerebral symptoms and serious sequelæ, this condition is considered to be due to shock. Chronic myocardial lesions or an insufficiency of the adrenals may cause sudden death during the performance of one of these operations on the chest wall. A similar clinical picture is seen in embolism of the pulmonary artery. Death accompanied by these signs may occur also in a few cases of emboli in the brain following thrombosis of pulmonary veins. It was demonstrated by experiments that we do not have a pleural reflex even in the normal pleura, which would explain these complications. They are proved by the accidents in pneumothorax therapy to be due to air emboli. The pathologic condition of the lung and of the pleural sheaths is the same in all these cases. The lung tissue shows in a circumscribed area a condition which is partly an infiltration, partly an induration of the tissue where the bloodvessels, especially the veins with their weaker walls, are fixed in a distended position.

An Experimental Study of the Ureter after Nephrectomy.—LATCHEM (*Jour. Urol.*, 1922, **8**, 257) finds that in the normal ureter after nephrectomy no attempt is made toward obliteration of the lumen by disappearance or atrophy of the mucous membrane; there is a noticeable

atrophy of the muscular coat. Hydronephrosis developed in every case following the production of complete obstruction of the ureter, the condition progressing to complete destruction of the substance of the kidney unless the obstruction was removed. The ureter after complete obstruction becomes a hydroureter by distention of the ureteral lumen with the retained urine. Hypertrophy of the muscular layers, chiefly of the circular, occurs. In the hypertrophic hydroureter or pyoureter with drainage of its contents after nephrectomy, the mucous membrane remains intact and the muscular coat gradually atrophies. In hypertrophic hydroureter or pyoureter with complete obstruction to drainage of the ureteral contents after nephrectomy, the mucous membrane remains intact and the muscular coats remain hypertrophic. Absorption of the contents of a distended ureter is very limited if it occurs at all. If infection is present in the contents of the ureter, it may spread through the wall and give rise to perureteral infection and abscess formation.

Some Experiences with the Meltzer-Lyon Test in Gall-bladder Disease.—CUTLER and NEWTON (*Surg., Gynec. and Obst.*, 1922, **35**, 146) think that there is still much to be proven before the so-called Meltzer-Lyon test can be accepted as of value in aiding diagnosis, for it is only in the experimental stage. The test depends upon the law of contrary innervation, which must be proven before the test is accepted. At the present time evidence would seem to show that syphonage is the principal factor in the dejection of bile into the duodenum. It is the authors' opinion that dark bile comes from the gall-bladder, for dark bile has never been found in cholecystectomized cases. The contentions of Einhorn and Meyer, that the dark color is due to reëxcretion of the salt or to destruction of red blood cells in the liver, with the production of excess iron, must bear further study. The authors' experience has given the distinct impression that the test is not of dependable diagnostic aid.

Tuberculosis in Children from the Standpoint of the Surgeon.—BROWN (*Boston Med. and Surg. Jour.*, September 28, 1922, p. 470) says that at present there are no accurate statistics in Massachusetts as to the number of nonpulmonary cases of tuberculosis and this lack is due to failure of hospitals and physicians to report their cases. Surgery in tuberculosis is and should be the exception and that it should always be made only an incident in the general and necessarily prolonged treatment. In children operations for spinal immobilization are not advisable, and without the proper postoperative care in adults do not give the results claimed. Ambulatory and supportive treatment both in adults and children have not given satisfactory results. The ideal treatment for children is recumbency, for at least two to three years, followed by carefully observed and protected weight-bearing for two years more. For adults in selected cases the operation for spinal immobilization may be advisable if it can be followed by at least six months of recumbency and a year or more of supportive treatment. In Massachusetts there are no hospitals, however, with equipment or personnel which can adequately carry out the prolonged treatment of recumbency and heliotherapy.

PEDIATRICS

UNDER THE CHARGE OF

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Dried Milk Powder in Infant Feeding.—CLARK and COLLINS (*Public Health Reports*, 1922, **40**, 2417) studied 319 infants. Of these, 241 were under observation a sufficiently long time to furnish reliable data for use in tabulating weights. No infant was included in the tabulation of results unless there was a record of weighing for at least four weeks; but in most cases the observations extended over a much longer period. Those babies fed on grade "A" milk were included in a group called Group I. In Group II there were those infants fed on reconstituted whole-milk powder. Considerable difficulty was experienced by the workers to gain the consent of the mothers to place infants on the reconstructed milk made from skimmed-milk powder and butter fat, for which reason Group III comprised a far smaller number. It was difficult to educate the mothers to this new form of infant-feeding. It was also difficult to get them to use this preparation, as the failure to procure a perfect emulsion made a certain collection of fat in the top of the bottles which did not appeal to them. In all age classes the infants fed on a modification of cows' milk made distinctly less progress as measured by gain in weight than those fed on a modification made from whole-milk powder. The difference was especially marked in the younger group—from one to three months old. The infants fed on a modification reconstructed from unsalted butter and skimmed-milk powder increased less rapidly in weight in the older groups and in the total groups; but in the younger age group the gain in weight closely approximated that of infants on whole-milk powder for about eleven weeks. After the twelfth week on this diet the rate decreased and the weight curve approached that of Group I. Because the weight curves for Group I were consistently below those for Group II for all age groups, the authors felt safe in concluding that the infants fed on whole-milk powder gained in weight more rapidly than did those fed on cows' milk. On account of the small number in Group III no definite conclusions were attempted. As regards scurvy, they feel that protection is dependent upon the antiscorbutic content of the particular dried milk used. The dried milks vary in this way in just the same manner that fresh milks do. To safeguard against the developing of this condition, orange juice or some similar material rich in antiscorbutic vitamine should be given routinely. The relation of the diet to rickets is much more complicated. It has been shown that some of the dried milks are as rich in antirachitic factor as cows' milk. A complete examination was made in 200 of these infants enrolled for this study and special attention was directed toward the incidence of rickets. One of the important points brought out by these examinations was the frequency and the similar distribution of

this disorder in the different feeding groups. A number of these infants undoubtedly presented a slight degree of rickets at the time of enrollment, but on account of the relatively short period of observation of the individual cases it was impossible to state with positiveness the effect of dried-milk feeding on the course of this disorder. It is important to note that the infants studied were recruited from homes of varied economic and hygienic status, and were fed on milk products containing fat in the usual percentages. This seems to indicate that other factors than the deficiency of fat-soluble vitamine must be taken into consideration in any attempt to determine the true cause of rickets. The writers feel as a result of their observations that dried-milk powders and their remade products, such as were used in this study, are safe for infant-feeding, and in some cases seem to have distinct therapeutic effect.

Rabbit Hair Asthma in Children.—RATNER (*Am. Jour. Dis. Child.*, 1922, **24**, 346) says that rabbit hair as an etiologic factor in the production of asthma would at first hand appear to be of little practical significance. As a matter of fact, its distribution is widespread, and it should be placed second to horse hair as a causative agent in the keratin group of asthma. Desensitization of this group of cases has not been successful, but the removal of the hair is easily accomplished, and avoiding the hair relieves the patient of all symptoms. In attempts at desensitization, the writer calls attention to certain dangers inherent in this form of treatment, and adrenalin should always be kept on hand to combat any emergency that may arise. Dosage undoubtedly plays a large part in the production of attacks. Human beings are capable of showing what might be called temporary desensitization. Eczema, vomiting, angioneurotic edema, urticaria and conjunctivitis may all occur as direct result of contact with animals besides the classic symptoms of asthma. In the way of prophylaxis it is recommended that rabbit hair and all fine dust-producing substances be kept out of pillows, mattresses, clothing and toys that are used for infants and young children. Those suffering from chronic coryza should be studied from the standpoint of their being potential asthmatics.

The Food Requirements of Children: Percentage Distribution of Calories.—HOLT and FALES (*Am. Jour. Dis. Child.*, 1922, **24**, 290) emphasize the importance of the balanced ration. The protein need of the growing child is very important and there seems to be a fairly general understanding of the amount required. All evidence seems to indicate than when 15 per cent of the theoretical total caloric need is supplied by protein, the nutritive needs in protein are met. The amount of fat required is still a subject of debate, but it seems reasonable and desirable that the amount of fat given the growing child should be equal to the amount of protein. Since fat has two and a quarter times the caloric value of protein, equal amounts of fat and protein would supply calories in the proportion of 2.25 to 1. When the protein furnished is 15 per cent of the total calories, an equal amount of fat would furnish about 35 per cent of the total calories. The remaining caloric need of 50 per cent would then be supplied by the carbohydrate.

When this distribution is deviated from, to any marked degree, for a long period of time, or when the proper balance of the diet is disturbed, various undesirable results may follow. If the protein is reduced much below 15 per cent of the caloric requirement, the nutritive need may not be met. If the fat given supplies much less than 35 per cent of the total caloric requirement, it usually happens that the caloric intake is excessive in carbohydrate and digestive disturbances usually follow. If the fat supplies too high a proportion of the total caloric requirements the fat tolerance of the child may be exceeded, and digestive upset may result. High fat with low protein forms a food from which constipation is likely to result. Low fat with high carbohydrate is apt to cause diarrhea.

Studies on Experimental Measles.—Duval and D'Aunoy (*Jour. Exper. Med.*, 1922, **36**, 239) obtained defibrinated human blood from measles cases at the stage of high temperature. This was inoculated into experimental animals. Their results show that an active transmissible virus exists in the blood of measles patients during the eruptive stage of the disease. The virus produces in rabbits after intravenous injection a specific reaction analogous in all essential features to that of the human infection. Repeated passage of the virus of measles through rabbits seems to increase its virulence. It is a noteworthy fact the pneumonia, so common in the fatal cases of human measles, was not evident in any of these experimental animals. The authors believe this to be of considerable significance, especially in elucidating the direct etiologic factor of the fatal pneumonias so often present in human measles cases. Apparently such infections in man can be explained purely on the basis of the destruction of normal defense barriers by the specific excitant of the infectious disease, and the lack of host resistance to the ordinary pyogenic bacteria.

Defects in School Children.—Bruce (*Brit. Med. Jour.*, 1922, **2**, 346) found that 58 per cent of the crippling existing at five years of age in 15,605 school children was due to rickets, and usually to rickets of the more severe type. The next most frequent cause of crippling was tuberculosis, which caused 9 per cent of the total crippling. He found comparatively little pulmonary tuberculosis. Routine medical inspection revealed no evidence of definite pulmonary tuberculosis, and only 7 suspected cases of the large total of 15,605 children examined. Chronic bronchitis was responsible for 6 per cent of the crippling found at this age. Mental deficiency comes next in the order of frequency, with 6.3 per cent, after nervous disorders with a percentage of 7.4. The cases of anemia and malnutrition, which account for 3.9 per cent of the total crippling, are those which showed no symptoms of other disease. In some of the cases a tuberculous family history could be elicited. The remaining 9 per cent of crippling was due to eye conditions, mostly strumous ophthalmia, a few cases of heart disease resulting from scarlet fever or rheumatism and other congenital and acquired deformities.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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Ulceration of the Female Genitalia.—PLANNER and REMENOVSKY (*Arch. f. Dermat. u. Syphilol.*, 1922, **140**, 162) describe cases illustrative of gonorrheal, aphthous and typhoid ulcerations of the female genitalia and of ulcerative lesions associated with erythema nodosum. The gonorrheal ulcer is the occasional sequel of perforation of a concealed Bartholin abscess through the labium, with involvement of the connective tissue, resulting in ulceration suggesting soft chancre. The gonococcus can be cultivated from the discharge from the ulcer base. It is often difficult to demonstrate the sinus-like connection with the gland. The authors insist that the term aphthous should be reserved for lesions of the vulva, in which no distinct etiologic factor can be recognized. The vaginal mucosa as well as the vulva may be involved and the eruptive outbreak preceded by a chill and high fever. Successive crops may occur, each associated with the same constitutional manifestations. Lesions of this type have been associated with erythema nodosum and with outbreaks of stomatitis. Bacteriologic investigation gives no characteristic findings. The authors describe a case of necrotic ulcer of the genitalia, associated with typhoid fever, in which typhoid bacilli were repeatedly recovered from the discharge from the lesions. The fourth group described includes 4 cases of tumor-like and ulcerative lesions of the genitalia, in 2 of which patients had demonstrable tuberculosis, and in 3 of which the lesions of erythema nodosum, associated with purpura and arthritic manifestations, were present. A similar case has been described by Jadassohn in 1904.

Hematogenous Distribution of Trichophyta.—BRUUSGAARD. (*British Jour. Dermat.*, 1922, **24**, 150) discusses the hematogenous distribution of trichophytic organisms and describes a case of kerion celsi in an elderly man, in which erythema multiforme-like lesions appeared upon the extremities. From these lesions tissue was obtained, in which it was possible to demonstrate the presence of trichophytic spores in the bloodvessels. Cultures from the fresh tissue showed the organism to be Trichophyton gypsum. The work of Bloch, Guth and others have shown that the deep pustular trichophyton infection of the skin is not infrequently associated with the development of eruptions, often follicular in character and general in distribution or nodular and localized on the extremities in certain cases, which strongly suggest a hematogenous distribution of the infecting agent. Immediately following the appearance of the Bruusgaard report, PASINI (*Arch. f. Dermat. u. Syphilol.*, 1922, **140**, 369) refers to Jessner's report in the same journal (1921) of the cultivation of Trichophyton gypsum from the blood of a boy, aged ten years, with an extensive lichenoid tri-

chophytid of the body. He states that Ambrosoli has also succeeded in cultivating Trichophyton gypsum directly from the blood in a boy, aged eleven years, with kerion of the scalp, just at the time the patient was developing a lichenoid trichophytid. It appears that this group of observations substantiates the hitherto theoretical conceptions of the hematogenous trichophytic origin of the so-called trichophytids. Apart from its independent interest as an immunologic and bacteriologic fact, the direct cultivation of the responsible organism from the blood in an eruption clinically so closely homologous with certain tuberculids, is a point of much significance and encourages the belief that improved cultural methods and earlier observation of cases will ultimately conclusively demonstrate the presence of tuberculosis bacilli in the circulation of patients with certain types of tuberculids. Moreover, as Bruusgaard remarks, these observations remove the deeper trichophyton infections from the domain of purely local to that of systemic disease.

Intramuscular Administration of Arsphenamin.—The revival of interest in intramuscular injection as a mode of administering arsphenamin derivatives is expressed in several recent articles. VOEGTLIN, DYER and THOMPSON (*Am. Jour. Syph.*, 1922, **6**, 576) cite Ehrlich's beliefs that intravenous use of these drugs should be regarded only as a means of avoiding the pain and inconvenience of the intramuscular technic. They quote Craig and Harrison as demonstrating a better effect of the latter method on the Wassermann, and cite also Voegtlin and Smith's demonstration of the superior trypanocidal effect of intramuscularly as compared with intravenously administered arsphenamin. The authors have conducted an experimental study of a derivative of arsphenamin closely related to neoarsphenamin (French trade name *sulpharsenol*), which they find is much less productive of local irritation even than neoarsphenamin when injected subcutaneously. Its trypanocidal effect is only slightly less than that of neoarsphenamin, its toxicity about equal to that of neoarsphenamin. It is very soluble and stable in solution, and produces little or no local irritation in the rat or rabbit in concentrations as high as 20 per cent in distilled water. The rate of excretion of the arsenic is about the same as that of arsphenamin and neoarsphenamin. The authors urge a more extended clinical trial of the drug as well suited to the needs of the general practitioner and possessing the advantages of intramuscular use without the disadvantages.

Comparisons of Arsphenamin and Neoarsphenamin.—The clinical differences between arsphenamin and neoarsphenamin, particularly with respect to therapeutic effectiveness, are illuminated by the report of VOEGTLIN and MILLER (*Public Health Reports*, 1922, **37**, 1627) on a series of comparisons of the parasitic value of the two drugs. The trypanocidal index was used because of its greater dependability as compared with the variability of syphilitic infections in experimental animals. The authors compared thirteen lots of arsphenamin and fifteen lots of neoarsphenamin of different manufacture, most of them recent products. The trypanocidal power of arsphenamin is remark-

ably constant in contrast with the very great variability of neoarsphenamin. Both drugs showed a considerable variability in toxicity, with a distinct reduction as compared with the products made two years ago. The authors point out the very interesting parallel relation between increased toxicity and increased therapeutic effectiveness, which seems to indicate that the reaction-producing power of a given lot of the drug is by no means necessarily a reason for discarding it. The comparison between the two drugs is certainly distinctly in favor of arsphenamin as the more constant and dependable preparation. The wide use of neoarsphenamin would seem then to be a matter of convenience rather than of intrinsic merit.

OPHTHALMOLOGY

UNDER THE CHARGE OF
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Ill-effects of the Arsenobenzols. — MEYNIARD (*La clin. ophthal.*, August, 1922, p. 319) calls attention to the occurrence of fatal or grave accidents from the arsenobenzols, notwithstanding that these substances have been in use now for more than ten years and the technic of their employment greatly improved. These ill-effects may be due to the administration of an ill-preserved product, polluted water, excessively warm syringe, faulty sterilization, failure of preliminary fasting and resting, contraindications overlooked, injection pushed too rapidly. [Improper hydrion concentration.—ED.] Very frequently, however, accidents occur in spite of every precaution; these are then usually attributed to intoxication, an occurrence which unfortunately is still inevitable in the present state of our knowledge; or to inferior quality of the agent, responsibility for which rests upon the manufacturer, as it is impossible for the physician to gauge the exact composition of the medicament. It is to be hoped that chemical and biologic standardization of these substances may be rigorously carried out before they are furnished to the practitioner.

Hereditary Optic Atrophy (Leber's Disease).—LAGRANGE (*Arch. d'ophthal.*, September, 1922, p. 530) concludes that it has not been proven that Leber's hereditary optic atrophy is due to defective development of the skeleton (optic foramen, sphenoidal cells) acting mechanically upon the retrobulbar portion of the optic nerve. Fischer has drawn attention to the relations which may exist between the development of the endocrine system and hereditary optic atrophy; but his hypothesis of the mechanical effect exerted by an overgrown hy-

pophysis or an enlarged sella turcica upon the adjacent optic nerve is unsatisfactory. In fact, in this disease the semeiology (white atrophy of the papilla, which is never one of stasis and always preserves its sharp contour with symptoms of retrobulbar neuritis) is clearly a syndrome, the opposite of that caused by intracranial tumors (papillary stasis) and in particular to juxtachiasmatic growths (temporal hemianopsia). In a case observed by the writer the blood presented a notable anomaly: Retarded coagulation with feebly retractile clot. It is remarkable that this particularity is precisely the stigma of hemophilia; now hemophilia and Leber's disease are comparable by their common character as hereditary diseases; the retarded coagulation in hemophilia may be considered as a simple stigma rather than as a symptom of pathogenic value. Without denying the numerous influences which may favor the occurrence of Leber's disease, in particular the associated influence of chronic intoxication nor unmindful of the obscurities which surround the pathogeny of this hereditary malady, early endocrine opotherapy deserves a place as a treatment of choice.

Primary Intraneural Tumor (Glioma) of the Optic Nerve.—VERHOEFF (*Arch. Ophthal.*, 1922, **51**, 120, 239) publishes a histologic study of eleven cases of intraneural tumors of the optic nerve. His conclusions are that the most common tumors of the optic nerves are gliomas—in fact the only primary intraneural tumors of this nerve that have been observed. These tumors are composed of three main types of neuroglia which may grade into one another. Some tumors consist of all three types; rarely does one consist of a single type. Tumors, in which so-called spindle cells predominate, contain the largest and most conspicuous neuroglia fibers. The spongy structure often displayed by these tumors, which at times has led to a diagnosis of myxoma, myxoglioma or myxosarcoma, is not the result of myxomatous degeneration, but is produced by excessive vacuolization of a neuroglia syncytium. Cysts of various sizes, which also often occur in these tumors, are due to the same process. The tumor is probably essentially congenital in origin and dependent upon some abnormality in the embryonic development of the neuroglia of the optic nerve. The growth stimulates proliferation in all contiguous neuroglia tissue, and thus causes the latter to take on the character of tumor tissue. The theory that tumors of the optic nerve stem are related in origin to neurofibromas of the peripheral nerves is, at present, founded on insufficient evidence, but cannot be dismissed as impossible.

The Influence of Trauma Upon the Onset of Interstitial Keratitis.—BUTLER (*Brit. Jour. Ophth.*, September, 1922, p. 413) concludes that an attack of interstitial keratitis may be precipitated by an accident to a cornea which is disposed to the disease by syphilis or tubercle; such trauma may be very slight, even the instillation of drops or the irritation of a general anesthetic. The attack in the injured eye is liable to be followed by the same disease in the uninjured eye, or the injury to one eye alone may cause interstitial keratitis in the other eye; in fact is it not possible that in every case of interstitial keratitis the disease is precipitated by some slight trauma?

The Lachrymal Fluid.—Rotth (*Klin. Monats. f. Augenhk.*, April-May, 1922, p. 598) discusses the question whether the properties of the tears vary according as the stimuli which calls them forth is different. His conclusion is that the index of refraction of the fluid secreted under the same stimulus varies within wide limits in the same person as also in different individuals; these variations in all probability depend upon the admixture of varying amounts of conjunctival secretion. When the tests are made with anemic conjunctivæ results are more uniform; in this case it is the secretion of the lacrymal gland alone. The index of such portions as are gathered after different stimuli also varies considerably, but the average values are quite concordant, showing that the lachrymal secretion from various stimuli is chemically identical in healthy eyes.

Ocular Complications of Pneumonia and Bronchopneumonia.—Villard (*Annal. d'oculist.*, October, 1922, p. 746) observes that of the various complications occurring in the course of pneumonia and bronchopneumonia, the ocular complications are the least known. He has been unable to find any mention of their occurrence in any work which he has consulted except two short paragraphs in the French *Encyclopedia of Ophthalmology*. From a lengthy study of the subject, he draws the following conclusions: In the course, or during the decline of pneumonia and bronchopneumonia there may supervene upon the part of the ocular apparatus an entire series of complications, rare indeed, but not so exceptional as to justify their entire neglect in classic works. The ocular complications are both extra- and intrabulbar. Among the former the least common are those which affect the conjunctiva, optic nerve and motor nerves, while the most frequent affect the cornea. These keratids may arise in the course of pneumonia, but more frequently complicate a severe bronchopneumonia, especially those occurring in the course of measles. They may take the form of an ordinary hypopyon keratitis, interstitial keratitis or a true keratomalacia; the prognosis is extremely unfavorable, resulting ordinarily in the loss of vision of the affected eye; in all probability, such keratids are due to an exogenous infection from the fingers or handkerchiefs soiled by expectoration in patients whose resistance has been lowered by the pulmonary affection. The intrabulbar complications may affect the iris, retina, the media and the deeper membranes of the eye. On the part of the iris there occurs exceptionally a true iritis, or more commonly, inequality of the pupils, the larger one corresponding to the side of the affected lung. Ophthalmoscopic examination shows inflammatory lesions of the retina, described by the author under the name "septic retinitis;" the lesions resemble tuberculosis of the retina and have a favorable prognosis. The media and deep membranes are at times gravely affected by lesions described under the name "metastatic ophthalmia;" this occurs in two forms: More rarely as a plastic iridochoroiditis, but most frequently as a suppurative iridochoroiditis, *i. e.*, a true panophthalmitis; this last affection is of endogenous origin, due to embolism of pneumococci which invade the vessels of the retina or perhaps those of the uveal tract.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Bacteriology of Human Cystic Bile.—In a series of 408 specimens of human bile, submitted by the surgeon at the time of cholecystostomy or recovered from the removed, intact gall-bladder shortly after operation and cultured, routinely, on plain serum broth with subsequent segregation of colonies on human blood-agar plates, isolation on slants and identification on appropriate carbohydrate fermentation "sets," RICHEY (*Penn. Med. Jour.*, 1922, **26**, 4) found pathogenic microörganisms in 173, or 44 per cent. The types of bacteria isolated fell within well-known groups, of which Bacillus coli was the most frequent (27 per cent), although due significance was given to Bacillus typhosus (7.4 per cent) and Bacillus paratyphosus (1.8 per cent) as well as to the other members of the colon-typhoid group. The Bacillus mucosus capsulatus group was responsible for 11.5 per cent of the positive cultures. Green streptococci (11.5 per cent) occurred twice as frequently as hemolytic streptococci (5.6 per cent), while staphylococci comprised 13.4 per cent. The author believes that the types of bacteria isolated, their relative incidence and usual habitat can be made to corroborate the statement of the experimental investigators that the two most important portals of entry of bacteria to the gall-bladder are the hematohepatogenous and the hematogenous, of which the former is the more frequent and important.

Complement-fixation in Typhoid Fever.—Although typhoid fever was one of the first diseases in which the phenomenon of complement-fixation was demonstrated, the field has not been explored extensively since the original endeavors of Bordet and Gengou. HADJOPOULOS (*Jour. Infect. Dis.*, 1922, **31**, 226) applied this test to 50 cases of typhoid and over 100 control cases. The complement-fixations were controlled by blood cultures and agglutination tests. Fresh human serum was placed in six pairs of small test-tubes in doses of 0.01, 0.02, 0.03, 0.04, 0.05 and 0.1 cc respectively. The left-hand series of tubes received 0.5 cc salt solution each and served as controls for the hemolytic value of serum in question. The right-hand tubes received 0.5 cc of the bacillary antigen each. After incubation at 37° C. for thirty minutes, 0.5 cc of 0.5 per cent suspension of sensitized sheep cells was added to all tubes. To those serums which were deficient in hemolytic value, a typhoid negative serum of high hemolytic value was added and the test carried on as usual. As a nucleus for antigen, eight or ten vaccines

were collected from various sources. By enriching this from time to time with strains from cases with a positive blood culture and negative complement-fixation, an antigen was obtained which would detect at least 80 per cent of cases in all stages of disease from the first to the fifth week. In 50 cases of typhoid and over 100 control cases it was found that the percentage of positive blood cultures was higher during the first week than the complement-fixation or agglutination tests, but, with the beginning of the second week the blood-culture curve fell abruptly, the immune reaction curves rose steadily, the fixation curve always preceding. During the fourth week of the disease the agglutination curve reached its peak at 88 per cent, tending to fall thereafter, whereas the complement-fixation curve, from the fourth week and on, stood at 100 per cent. The pathologic conditions giving rise to nonspecific complement-fixation, excepting 1 case of typhus, clinically also could be differentiated from typhoid. On the other hand, nonspecific agglutination occurred in almost 100 per cent of acute infectious diseases as typhus, malaria, miliary tuberculosis, acute mastoiditis, acute appendicitis and influenza, that could not be easily differentiated from typhoid without further clinical and laboratory data. The authors believe that "In the course of typhoid infection the formation of complement-fixing antibodies is one of the earliest and most constant immune manifestations."

The Incubation Period of Typhoid Fever.—It is recognized generally that the incubation period of typhoid fever cannot be determined accurately, as a rule, as the exact date of infection is not known. MINER (*Jour. Infect. Dis.*, 1922, **31**, 296) has analyzed eleven reported typhoid fever epidemics in which the time of infection could be definitely established and in which, therefore, the distribution of the incubation period could be determined. By calculating the results of the various investigators with mathematical precision, it was found that the results were consonant with the belief that the length of the incubation period depends in part on the virulence of the infection and is extremely variable, ranging from three to thirty-eight or forty days. The mean incubation period in the different epidemics varied from 7. ± 0.26 to 19.5 ± 0.31, whereas the means for those due to infected food, in which the dose was in all probability more massive, were 7. ± 0.26 and 9.54 ± 0.39.

The Meiostagmin Reaction.—"The meiostagmin reaction (*meion*, small; *stasso*, drop) is the name given to a phenomenon, which involves a lowering surface tension during incubation when a diluted serum, containing certain antibodies, is mixed with its specific lipoid-containing antigen. First employed by Ascoli, working with alcoholic extracts of typhoid bacilli, the reaction was later applied by Ascoli and Izar to the diagnosis of certain malignant tumors with rather indifferent success. Like similar physicochemical reactions the method has not been used extensively by physicians, although several investigators have reported conflicting findings which have served to throw doubt on the procedure as to its efficacy. Recently GOUWENS (*Jour. Infect. Dis.*, 1922, **31**, 237) conducted over eleven hundred tests

in a study of this reaction, using almost two hundred different mixtures of rabbit serum and antigen. The serum was obtained from animals immunized against Bacillus paratyphosus B, and the antigens were prepared from homologous and several heterologous organisms, as well as from the liver of a healthy rabbit immune to Bacillus paratyphosus B. In making the tests it was found that the Du Nouy surface tension apparatus gave readings with the biochemical mixtures employed, which were as accurate as those obtainable with the more cumbersome and slow drop weight apparatus, while the sources of experimental error were less than those involved in the use of the Traube stalagmometer. The spontaneous surface tension changes and the limits of experimental error were as great as when relatively dilute serum was used as when the serum was diluted only 1 : 20, the blood serum being responsible for the relatively large error. The meiostagmin reaction did not reveal the presence of antibodies in Bacillus paratyphosus B immune rabbit serum of high titer regardless of the dilutions in which the serums and antigens were employed or of the solvents used in the preparation of the antigens.

The Hydrogen-ion Concentration of Joint Exudates in Rheumatic Fever and Other Forms of Arthritis.—In order to compare the reactions of the exudates in certain arthritic diseases and to determine whether an acidity occurs in the inflamed joints in acute rheumatic fever sufficient to permit the liberation of free salicylic acid following salicylate therapy, BOOTS and CULLEN (*Jour. Exper. Med.*, 1922, **36**, 405) ascertained the hydrogen-ion concentration of 26 joint fluids including 16 from patients with acute rheumatic fever, 7 of undetermined origin and 2 with bacterial arthritis. In each instance the fluid was aspirated by means of a Luer syringe, care being taken throughout the entire determination to prevent the fluid from coming in contact with air. When large quantities of fluid were available both electrometric and colorimetric p^H determinations were made, although only the colorimetric method was used in the majority of cases. The electrometric measurements were conducted at 38° C. in the Clark cell, in a hydrogen atmosphere containing CO_2 at the tension existing in the joint fluid, while the colorimetric determinations method was that described by Cullen for the determination of the p^H concentration of blood. The joint fluids in the acute rheumatic fever patients were never frankly purulent, being viscous, slightly to definitely turbid and usually of a pale yellowish green color. The exudates contained considerable fibrin, forming soft clots on standing. Bacteriologically they were all sterile by ordinary culture methods. The fluids from the cases with arthritis of undetermined origin were indistinguishable from some of these exudates. It was found that, "With the exception of the joint exudates of the 2 patients with bacterial arthritis, the reactions were all slightly alkaline and approximated the normal reaction of blood," varying between p^H 7.27 and 7.42 in acute rheumatic fever and between p^H 7.33 and 7.47 in those arthritides of undetermined origin. The exudate from the knee-joint infected with Staphylococcus aureus was p^H 6.69 and from the one with Streptococcus hemolyticus, p^H 6.19, both being distinctly acid. The effusion from

the patient with anasarca of myocardial insufficiency was p^H 7.34. The authors state that they have evidence to show that the exudates in experimental arthritis of animals inoculated with green streptococci are also acid and from their results "It would seem that if green streptococci were growing in the joint fluids of rheumatic fever patients, one would expect those fluids to be acid," which, as they have shown, is not the case. They conclude that "Since a definitely acid medium is necessary for the liberation of free salicylic acid and since all of the joint fluids from patients with acute rheumatic fever were slightly alkaline, no free salicylic acid could possibly exist in such joint fluids following the administration of salicylates."

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Use of Semilogarithmic Paper in Plotting Death Rates.—WHIPPLE (*Public Health Reports*, 1922, **37**, 1891) emphasizes the advantage of semilogarithmic paper (vertical scale based on logarithms, horizontal arithmetical) and presents graphs showing the movements of many diseases since 1870. Pneumonia remains relatively constant, save for large excursions due to epidemic influenza. Tuberculosis has shown a steady decline, interrupted by a rise due to influenza also, but the present mortality stands at about one-fourth that of 1870. Typhoid fever shows a decline in deaths from 100 per 100,000 to less than 3 in the same population unit. Diphtheria and scarlet fever have shown irregular, but, on the whole, marked declines, but this does not hold for measles or whooping-cough. Bright's disease, cancer and diseases of the circulatory system have been steadily increasing.

Preparation and Administration of Arsphenamine and Neoarsphenamine.—The U. S. PUBLIC HEALTH SERVICE (*Public Health Reports*, 1922, **37**, 1867) issues a series of instructions on the administration of the newer arsenicals. In general, the preference is given to arsphenamine over neoarsphenamine. High dilutions of the drugs are recommended and special stress is laid on the proper alkalinization of the arsphenamine. Slowness of injection is urged as being highly important in preventing reactions. Detailed instructions are given

covering preparation of solution and injection. (Reprints may be had by addressing the Surgeon-General, U. S. Public Health Service, Washington, D. C.)

The Posture of School Children in Relation to Nutrition, Physical Defects, School Grade and Physical Training.—STERLING (*Public Health Reports*, 1922, **37**, 2043) states: "The posture of school children cannot be said to depend entirely, or even chiefly, on any one condition. The following conclusions seem to be confirmed by the facts noted in this study: (1) While good nutrition is a contributing factor to good posture, it is by no means an indispensable condition. (2) Defective vision, adenoids and bad tonsils tend to have an unfavorable effect on a child's posture. (3) When the hygienic conditions in a school are not of the best, and health measures are inadequate, there is a moderate decrease of good posture and increase of poor posture from the first to the fifth grade, inclusive. This is not believed to be a necessary accompaniment of school life, but a condition that may be easily remedied by coöperation of the health and education authorities. (4) In planning exercise with a view to the promotion of good posture, it is suggested that setting-up exercises be simple and vigorous and play full of energy and vim. Formless, jellyfish gymnastics, or stupid, silly games, played half-heartedly, have little place in the proper physical development of the growing child."

Typhus Fever in Boston and a Review of the Newer Methods of Diagnosing Typhus.—SHATTUCK (*Am. Jour. Trop. Med.*, 1922, **2**, 225) states that the small number of cases of typhus, and of probable typhus, found in the records of the Boston City Hospital, covering the period of the past ten years, points to the conclusion that the typhus problem there has not been significant from the diagnostic standpoint. Nevertheless, the potential epidemiologic significance of typhus, and particularly of atypical cases, requires that all cases of possible typhus be studied with the greatest care in order to arrive, if possible, at a satisfactory diagnosis. Under the head of possible typhus are included a considerable group of cases having eruptions or temperature curves suggestive of typhus. This group is composed of two classes of cases: (1) Undiagnosed infections; (2) diagnosed infections, in which the diagnosis is not adequately supported by facts when recent advance of knowledge is taken into consideration. Careful investigation of all cases in which typhus might seem a possible diagnosis would perhaps show that typhus fever is in reality more common in Boston than it appears to have been in recent years. A Widal reaction positive in the dilutions generally used for diagnosis is commonly present in typhus fever and, therefore, it is not, *per se*, an obstacle to the diagnosis of typhus. The proteus reaction of Wilson, Weil and Felix is not infallible, but a very valuable aid to diagnosis. The proteus reaction to be of value must be adequately controlled. Not only should controls be performed with the test, but it would seem necessary from time to time to check, with known typhus serum, the agglutinability of the culture used for the test. For interpretation of the results of the test, all known facts regarding it should be borne in

mind and clinical evidence should be taken into consideration. Probably the surest means of diagnosing typhus fever during life is by means of histologic examination of excised bits of skin. Pathologic changes developing in the guinea-pig after inoculation, with material containing the virus of typhus, are believed to be constant, but may be difficult to demonstrate. Somewhat similar lesions due to other causes may perhaps lead to error. Guinea-pig inoculation may be used for diagnosis. The point of greatest importance for diagnosis in the blood picture is the almost constant absence of leukopenia in typhus and its nearly constant presence in typhoid. The cerebrospinal fluid shows an increase of cells which may be slight or marked. Failure to recognize this fact may lead to erroneous interpretation of the findings. Other changes usually found in this fluid are less important. Wiener's color reaction is very easily performed and seems to warrant further trial. Other tests and diagnostic points have not been shown to have considerable value.

The Relative Parasiticidal Value of Arsphenamine and Neoarsphenamine. — VOEGTLIN and MILLER (*Public Health Reports*, 1922, **37**, 1627) describe the technic of determining in an experimental way the therapeutic activities of members of the arsphenamine group, and conclude as follows: "The results obtained in this investigation confirm previous data from this laboratory to the effect that arsphenamine of different manufacture is fairly uniform in parasiticidal power, whereas neoarsphenamine shows great variations. The toxicity of the average commercial arsphenamine and neoarsphenamine manufactured at the present time is considerably lower than that of preparations found on the market two years ago. The technic of the trypanocidal test as elaborated in this laboratory during the last few years is described in detail."

The Weil-Felix Test for Typhus Fever.—HOLT-HARRIS and GRUBBS (*Public Health Reports*, 1922, **37**, 1675) have employed the agglutination test for typhus, using certain strains of the Proteus group in connection with maritime quarantine procedure and find it of great value. A positive reaction is regarded as diagnostic, and a negative one after three to seven days constitutes very strong evidence against the disease.

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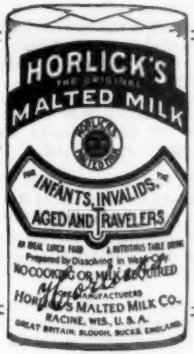

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